The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 113, No. 24 — COPYRIGHT, 1939, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS — DECEMBER 9, 1939

SOME CLINICAL NEUROLOGIC ASPECTS OF VITAMIN B DEFICIENCIES

CHARLES D. ARING, M.D.
JOSEPH P. EVANS, M.D.
AND
TOM D. SPIES, M.D.
CINCINNATI

Vitamin B_1 (thiamin, aneurin, catorulin) and nicotinic acid are the only components of the vitamin B complex which are known to be of significance in the maintenance of normal neurologic function in man (fig. 1). The use of these substances in the treatment of various neurologic diseases will be discussed in this presentation. A discussion of the diagnosis of the neurologic diseases incident to a deficiency of these substances must be slighted because of the limitation of space.

VITAMIN B_1

Neuritis.—Neuritis means disease of the neuron (Brown [1]). The principal causes of neuritis may be grouped under six inclusive headings, given in the accompanying table, as has been done by Cobb and Coggeshall.[2] As the causes of neuritis are better understood, such clinical classifications will be replaced by classifications based solely on etiology.

Localized Neuritis: This type of neuritis usually occurs in ambulatory patients, and the mechanical or infectious agent can often be determined by clinical methods. The symptoms usually respond to medical and surgical therapy. Relief of localized neuritis following the administration of crystalline vitamin B_1 has been reported by some investigators. Such reports, however, tend to be misleading, since physicians who obtain negative results are less prone to report them. Furthermore, the number of reported cases is small, and in general the studies have not been adequately controlled. Hence the results need confirmation. Likewise, no conclusive reports have as yet appeared in the literature concerning the value of vitamin B_1 in the prevention of localized neuritis.

We have observed the relief of the acute pain in a case of brachial neuritis occurring six weeks after mastectomy, with the use of daily intravenous injections of 50 mg. of vitamin B_1 [3] in sterile physiologic solution of sodium chloride for seven days.

Generalized Polyneuritis: Virus Polyneuritis. The virus diseases listed in the table are often characterized or accompanied by peripheral neuritis as a late complication. No crucial observations have been made to determine whether faulty nutrition plays a role in the development of the neuritis seen in these diseases. The small amount of experimental evidence available tends to show that vitamin B_1 does not play any direct specific role in counteracting the effects of these infectious agents.

Our experience with three cases of infectious polyneuritis has been that some of the neurologic symptoms have progressed despite large intravenous doses (50 mg. twice a day) of thiamin.

Bacteriotoxic Polyneuritis. The diseases in this group often interfere with proper nutrition and thus predispose the patient to the development of a deficiency of vitamins. Many patients with an infection also have an increased requirement for certain essential nutritive substances. In typhoid, for example, the requirement for vitamin B_1 is increased because of the fever, loss of appetite or excessive diarrhea. The incidence of peripheral neuritis in patients with typhoid was high a few decades ago, when an effort was made to restrict the diets of such patients. The great decrease in the incidence of peripheral neuritis in typhoid in recent years is probably due to prescription of adequate diets in the treatment of that disease. There is little information concerning the role of vitamin B_1 deficiency in the development of any of the neuritides accompanying bacteriotoxic diseases, but a number of reports have indicated that the administration of vitamin B_1 often relieves the symptoms of neuritis in these cases. It is known that the neuritis of certain persons with infectious diseases disappears after the administration of a well balanced diet.

The neuritis accompanying acrodynia possibly belongs under this heading. Durand, Spickard and Burgess [4] reported the cure of acrodynia in two children following intramuscular injections of vitamin B_1.

Chemical Polyneuritis. There are many chemical substances which may produce peripheral neuritis. Not every person exposed to the same chemical agent, however, responds in an identical manner. There is clinical evidence showing the predilection of some of these substances for special portions of the nervous system.

The course of two cases of triorthocresyl phosphate poisoning (jamaica ginger paralysis) shortly after the onset of symptoms was unaltered by the use of large amounts of crystalline vitamin B_1 by mouth. One of the

This work was supported by grants from the Rockefeller Foundation and the Charles E. Fleischmann Fund.

From the Department of Internal Medicine and Neurology and the Laboratory of Neuropathology, University of Cincinnati College of Medicine.

Read before the joint meeting of the Section on Pathology and Physiology and the Section on Nervous and Mental Diseases at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 19, 1939.

1. Brown, M. R.: Diagnosis and Treatment of Polyneuritis, M. Clin. North America **22**: 627-634 (May) 1938.
2. Cobb, Stanley, and Coggeshall, H. C.: Neuritis, J. A. M. A. **103**: 1608-1617 (Nov. 24) 1934.
3. Furnished by Merck & Co., Inc.
4. Durand, J. I.; Spickard, V. W., and Burgess, Ernest: Acrodynia Treated with Intramuscular Injections of Vitamin B_1, J. Pediat. **14**: 74-78 (Jan.) 1939.

patients received 20 mg. daily for one month, and the other received 500 mg. daily for the same length of time. It is theoretically possible that large amounts of vitamin B_1 crystals given before the ingestion of triorthocresyl phospate might act as a protective agent. It has been reported that the administration of vitamin B_1 causes relief of the symptoms of the neuritis following exposure to toxic agents such as nicotine, lead, thallium, arsenic and mercury. As yet, however, there is no conclusive evidence that the lack of vitamin B_1 plays a major role in the development of any of the "chemical neuritides."

We have noted improvement in a case of emetine neuritis following the administration of large doses of vitamin B_1, first given intravenously in sterile physiologic solution of sodium chloride and then by mouth. The relief was marked after the first day of treatment, and there was complete relief of symptoms at the end of the third month of treatment. We have been unsuccessful in relieving the neuritis of a young man, a worker with refrigerants. The most likely offender in this case was methyl chloride.

Nutritional Deficiency or Metabolism Polyneuritis. There is a long list of diseases in which polyneuritis, when it occurs, is conspicuously related to a lack of proper nutrition. This list is composed chiefly of metabolic and deficiency diseases, which often have a number of clinical features in common. In a presentation of this scope we are concerned chiefly with the neuritis manifestations of patients having any of these diseases.

Evidence is accumulating which indicates that many of the neuritic symptoms listed under various syndromes are clinical variations of one large etiologic group. Since vitamin B_1 will usually relieve the manifestations of the polyneuritis of beriberi, a known dietary deficiency disease, and since it is essential for the integrity of the nervous tissue in general, it seems likely that its absence may play a very important part in the development of neuritis in a number of these diseases in addition to berberi. Evidence indicates that vitamin B_1 is a useful therapeutic agent in the treatment of "alcoholic" neuritis, with or without pellagra, of the polyneuritis of pregnancy and of the neuritis associated with diabetes. Most of the other diseases under this heading are related to disturbances of nutrition, and it may be that a lack of vitamin B_1 plays a role in the production of the neuritic manifestations which so frequently accompany them. These diseases of metabolism are often associated with loss of appetite and malabsorption, conditions, which in themselves may lead to a deficiency of some specific factor or factors.

The clinical manifestations of these diseases are extremely variable. If one studies a large group of persons who are addicted to alcohol and who are also malnourished, it will be found that some have no symptoms, others have symptoms of beriberi, and others nervous, dermal and gastrointestinal symptoms characteristic of pellagra. Still others will show hematologic and neurologic changes similar to those associated with sprue and pernicious anemia. In some of the persons addicted to alcohol, Korsakoff's syndrome develops. This clinical syndrome is characterized by a peripheral neuritis which is identical with that of beriberi and by a psychosis often resembling the mental changes seen in pellagra.

We have had experience with the neuritis of pellagra, pernicious anemia, beriberi ("alcoholic and nonalcoholic neuritis"), tuberculosis and pregnancy. These neuritides, excepting possibly the neuritis encountered in pernicious anemia, respond promptly to large doses of vitamin B_1. We usually administer thiamin intravenously, giving 50 mg. twice a day for one week. The initial response to this treatment is usually rapid. Pain is usually greatly relieved within twenty-four hours, and strength, accuracy and speed of movement are usually improved within three days, this improvement possibly being due to the conspicuous relief of pain. If analgesics have been used they may often be discontinued at this time, and patients who have slept little or not at all for weeks may be able to sleep with no medication other than vitamin B_1. The relief which usually occurs in this group of nutritional deficiency neuritides is abrupt and dramatic. Patients previously

Principal Causes of Neuritis

Neuritis					
Generalized Polyneuritis				Localized Neuritis	
Virus	Bacteriotoxic	Deficiency or Metabolism	Chemical	Mechanical	Infectious
Measles	Focal infections	Pellagra	Mercury	Pressure	Diphtheria
Smallpox	"Rheumatism"	Pernicious anemia	Lead	Tumor	Tetanus
Chickenpox	Erysipelas	Sprue	Silver	Edema	Streptococci
Parotitis	Scarlet fever	Beriberi	Arsenic	Arthritis	Leprosy
Herpes	Rheumatic fever	"Alcoholic neuritis"	Phosphorus	Fibrosis	
"Acute febrile"	Chorea	"Korsakoff's psychosis"	Methyl alcohol	Trauma	
"Acute infective"	Septicemia	Pernicious vomiting	Ethyl alcohol	Saturday night paralysis	
"Landry's"	Puerperal fever	Hunger edema	Ethyl iodide	Volkmann contracture	
Poliomyelitis	Gonorrhea	Pregnancy	Trichlorethylene	Meralgia paraesthetica	
Encephalomyelitis	Meningitis	Chronic colitis	Carbon tetrachloride		
Epidemic (lethargic) encephalitis	Diphtheria	Cancer with cachexia	Trinitrotoluene		
Erythroedema	Typhoid	Tuberculosis with cachexia	Dinitrobenzene		
Acute rabic myelitis	Paratyphoid fever	Senility with cachexia	Triorthocresyl phosphate		
	Typhus fever	Diabetes	Aniline		
	Influenza	Myxedema	Sulfonethylmethane, barbital		
	Pneumonia	Hematoporphyrinuria	Chloral hydrate, chlorobutanol		
	Malaria	"Recurrent polyneuritis"	Carbon monoxide		
	Relapsing fever	"Chronic progressive polyneuritis"	Carbon disulfide		
	Serum sickness	Chronic bacillary dysentery	Thallium		
	Acute enteric fever		Sulfur		
	Syphilis		Emetine		
			Gold		
			Bismuth		
			Sulfanilamide		

bedfast may be able to walk within a few weeks. However, the patient quickly reaches a stage beyond which thiamin will not cause further improvement, and residual changes may persist indefinitely.

It is our thought that the initial prompt improvement with thiamin in cases of nutritional deficiency is humoral

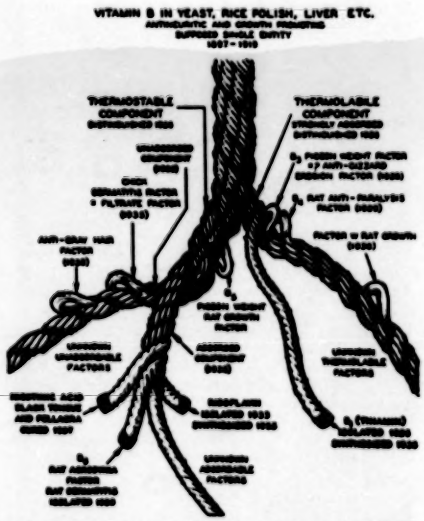


Fig. 1.—Differentiation of the components of the vitamin B complex. The components that have been isolated in a pure state are indicated in heavy lettering; those which have been recognized only by the discrepancies in physiologic properties of various crude extracts are indicated as loops; the possible, still unknown factors are divided into three main strands according to the principle of adsorbability, which has been so useful in differentiation experiments (from Williams and Spies, Vitamin B_1, New York, the Macmillan Company, 1938).

in nature. This impression is furthered by the work of Minz,[5] who has been able to show that vitamin B_1 enhanced the effect of acetylcholine in the transmission of the nervous impulse. It seems that vitamin B_1 inhibits cholinesterase in the same manner as does physostigmine. In our cases in which this test was performed (in vivo) the serum cholinesterase was inhibited by the administration of thiamin. Glick and Antopol [6] obtained similar results with horse and rat serum (in vitro), and they made the important observation that the inhibition of the serum cholinesterase was obtained only with concentrations of vitamin B_1 in excess of those known to occur in the living organism.

We have studied the peripheral nerve histologically by the biopsy method in twelve cases of deficiency disease with neuritic symptoms, in several instances both before and months after treatment with crystalline vitamin B_1. In all cases marked loss and degeneration of myelin sheaths was observed in the terminal portions of the internal branch of the anterior tibial nerve (figs. 2, 3 and 4). The axons in these peripheral nerves have been, on the whole, normal. In cases in which the peripheral nerve was examined as long as eleven months after treatment was instituted, the loss of myelin sheaths was severe.

This study lends support to the hypothesis that the initial spectacular improvement following vitamin B_1 therapy which is experienced by sufferers from nutritional neuritis is on a humoral basis. It also illustrates how slowly restitution of the nerve may occur.

In ten cases of moderate nutritional neuritis the administration of cocarboxylase [7] (phosphorylated thiamin), 10 mg. in sterile physiologic solution of sodium chloride twice daily by intravenous injection, resulted in the same improvement that had been seen following the use of thiamin. This result supports the hypothesis that vitamin B_1 may be utilized as cocarboxylase by the body.[8]

NICOTINIC ACID TREATMENT OF PELLAGRA

Mental changes as a part of the pellagra syndrome have been recognized by many physicians, and in areas where the disease is endemic these symptoms are so common and so striking that they have become associated with pellagra even by the lay observer. Various abnormal psychic states have been described in medical literature on pellagra, and some writers have thought that one or another psychosis was typical of this disease.

Subclinical pellagrins are noted for the multiplicity of their complaints, among which are many that are usually classified as neurasthenic. The most common of these symptoms are fatigue, insomnia, anorexia, vertigo, burning sensations in various parts of the body, numbness, palpitation, nervousness, a feeling of unrest and anxiety, headache, forgetfulness, apprehension and distractibility. The conduct of the pellagrin may be normal, but he feels incapable of mental or physical effort, even though he may be ambulatory.

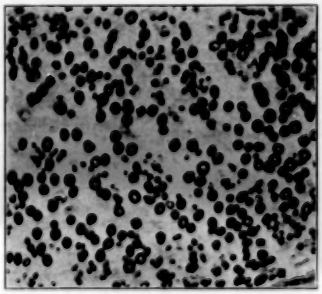


Fig. 2.—Biopsy section of the terminal portion of the internal branch of the normal anterior tibial nerve, stained with fresh 1 per cent osmic acid for from twenty-four to thirty-six hours; × 200. The normal myelin sheaths stain in clearcut circles.

The noticeable and more serious mental signs of pellagra manifest themselves in various types of psychoses. The most common is perhaps that in which loss of memory, disorientation, confusion and confabulation are predominant. There are also types in which excitement, mania, depression and delirium may occur.

5. Minz, Bruno: Le rôle de la vitamine B_1 dans la régulation humorale du système nerveux, Presse méd. **46**: 1406-1407 (Sept. 21) 1938.

6. Glick, David, and Antopol, William: The Inhibition of Cholinesterase by Thiamin (Vitamin B_1), J. Pharmacol. & Exper. Therap. **65**: 389-394 (April) 1939.

7. Furnished by Merck & Co., Inc.

8. Spies, T. D.; Aring, C. D.; Gelperin, Jules, and Bean, W. B.: The Mental Symptoms of Pellagra, Am. J. M. Sc. **196**: 461-475 (Oct.) 1938.

In our experience a paranoid condition is common in pellagrins. These patients, acting on their paranoid delusions, are more active than are other pellagrins with psychoses.

The acute psychoses of seventy pellagrins have been relieved quickly with the use of nicotinic acid (Spies, Aring, Gelperin and Bean [8]). The psychosis had been present from one to eighty-three days, and the psychosis of ten patients had been induced in the hospital. From 500 to 1,000 mg. of nicotinic acid was administered daily in 50 mg. doses.

The relief of the numerous and varied abnormal mental signs in this group of pellagrins was dramatic in its suddenness and was maintained as long as nicotinic acid or a well balanced diet supplemented with nicotinic acid was administered. In no instance were we unable to relieve the psychosis. Further experience has upheld the efficacy of nicotinic acid in the treatment of this type of patient.

In thirteen cases we were unable to relieve completely the chronic psychosis accompanying pellagra. Large doses (from 500 to 1,000 mg. daily) of nicotinic acid were administered for periods varying from one and one-half to two and one-half months to the pellagrins suffering from chronic psychoses. These patients became more alert, cooperative and tidy, and apathy and restlessness disappeared. Some of them changed from a bedridden to an ambulatory status. However, hallucinations and delusions usually persisted, although an occasional patient gained some insight into his condition.

Several reports (Evans,[9] Bogart,[10] Frontali and Ferrari [11]) have appeared on the beneficial effect of nicotinic acid in the psychosis of pellagra. There has been no report of the complete relief of a chronic pellagrous psychosis of many years' duration. For only one patient, who had been in a mental hospital for nine months, were we able to effect anything approaching complete cure. These cases are too few to serve as a basis for a final opinion.

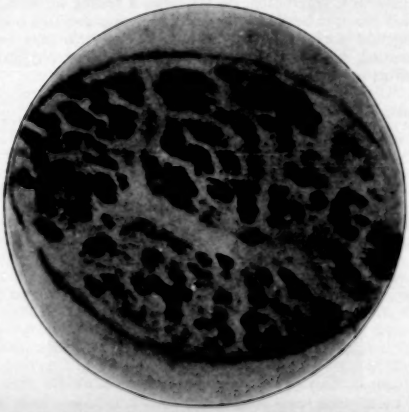


Fig. 3.—Section of the terminal portion of the internal branch of the anterior tibial nerve of a patient with alcoholic neuritis; × 1,225. There is loss of myelin sheaths. The myelin sheaths remaining are not regular in outline. Wide clefts appear in the substance of the bundles.

Nicotinic acid was also administered (Spies, Aring, Gelperin and Bean [8]) to a group of 225 mildly affected pellagrins with complete relief of their rather typical complaints, which have usually been considered to be those of neurasthenia. With nicotinic acid therapy the ambulatory pellagrin also regains energy and appetite. This relief occurs from one to twelve days after the administration of from three to six doses, 100 mg. each, of nicotinic acid a day.

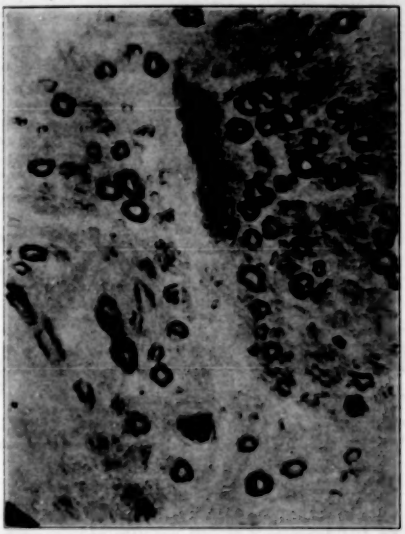


Fig. 4.—Section of the terminal portion of the internal branch of the anterior tibial nerve of a patient with alcoholic neuritis, ten months after thiamin therapy which had been continuous for two months; × 1,000.

(Nicotinic acid has been reported to have been used with benefit in Wernicke's disease [Jolliffe [12]]. Recent experimental work with animals and clinical observations have indicated that the lack of vitamin B_1 may result in Wernicke's disease and that this condition may be relieved by the administration of vitamin B_1.)

COMMENT

Vitamin B probably has been administered to patients suffering from every kind of nervous disease. Like other new medicaments (insulin, liver extract, sulfanilamide), it has been applied in the treatment of many diseases.

As far as the nervous system is concerned, the evidence suggests the following claims for vitamin B_1 to be allowable: It is of value in correcting and preventing beriberi and the neuritis that accompanies this disease; it is of value in the treatment of the neuritis associated with chronic alcoholism, pellagra and pregnancy. There is enough clinical information available

9. Evans, V. L.: Pellagra with Psychosis and Minimal Physical Symptoms, J. A. M. A. **113**: 1249-1250 (April 1) 1939.
10. Bogart, C. N.: Nicotinic Acid in the Treatment of Pellagra, J. A. M. A. **113**: 613-614 (Aug. 13) 1938.
11. Frontali, G., and Ferrari, G.: Le forme nervose della pellagra curate con acido nicotinico, Minerva med. **2**: 133-148 (Aug. 11) 1938.
12. Jolliffe, N. H.: Alteration of Mental and Emotional Processes by Vitamin Deficiency, read at the meetings of the Association for Research in Nervous and Mental Diseases, New York, Dec. 27-28, 1938.

at the present time to warrant the trial of thiamin for patients who have peripheral neuritis associated with dietary deficiency or undernutrition from any cause. Also a trial is warranted in peripheral neuritis and edema of undetermined origin.

Our experience with six patients suffering from severe pain (carcinoma, cord tumor, brachial and trigeminal neuralgia) was that thiamin administered intravenously in 50 to 100 mg. doses daily over a period of ten days did not act as an analgesic.

We are unable to evaluate the statements in the literature that other neurologic conditions may be improved with the use of vitamin B_1, but it is our belief that this vitamin is useful in the amelioration of these disorders only if they are caused by its deficiency. It is often difficult to make a clinical diagnosis of vitamin B_1 deficiency with any degree of assurance, but this defect may be remedied shortly by the development of simple diagnostic laboratory methods.

SPECIFIC THERAPEUTIC AND PREVENTIVE MEASURES

The vitamin B deficiencies can be greatly decreased by the application of the following recommendations:

1. Fresh foods, such as potatoes, native vegetables, pork and liver, eggs, milk, fruits and especially beans and whole grain cereals should be substituted for or added to a diet of decorticated cereals and dried or canned foods whenever possible.

2. The use of dried yeast, wheat germ, liver, kidney and vitamin B_1 crystals as supplements to the diet should be encouraged whenever possible. The expense of such materials, however, often interferes with their extensive use.

3. Since vitamin B_1 is water soluble, a large amount of it is lost when the water in which the foods are cooked is thrown away. It is recommended, therefore, that the water in which foods containing vitamin B_1 are cooked be used for broths. Whole barley or other grains which are rich in vitamin B_1 may be added to such broths to insure additional protection.

4. The use of undermilled rather than overmilled grains should be rigidly enforced among government troops and in prisons, asylums and other institutions where mass feeding is required. Each lot of grain purchased should be examined to determine whether there is an adequate amount of the germ and of the external layers of the grain. Since molds, weevils and other infestations deprive cereals of this vitamin, one must be certain that the grain has not spoiled.

5. Particular attention should be directed toward the diets of persons with chronic debilitating diseases and increased metabolism, for the incidence of vitamin B_1 deficiency is high among such patients. Alcoholic addiction, pellagra, sprue, pernicious anemia, colitis, diabetes mellitus, tuberculosis, senility, malignant tumor, cirrhosis and other diseases may interfere with the proper nutrition of the patient and thus predispose to the development of vitamin B_1 deficiency.

6. The diets of pregnant and lactating women should be especially rich in vitamin B_1. Whenever there is any doubt as to the adequacy or utilization of this vitamin either in the mother or in the child, supplements should be given. The supplements should be continued both in the mother and in the child until the proper diet is assured. The nursing mother should receive at least 5 mg. of thiamin or its equivalent daily; the infant should receive 0.5 mg. a day or its equivalent, and children should receive 1 mg. or its equivalent a day.

7. The requirement for vitamin B_1 may be distinctly above the average in persons with fever, severe gastrointestinal symptoms, hyperthyroidism and other conditions. It is essential for the physician to prescribe amounts above the average for such persons. We suggest a maintenance dose, from 5 to 10 mg. of pure vitamin B_1 or its equivalent a day, except when the patient is unable to absorb from the gastrointestinal tract. In such instances it is essential that vitamin B_1 be given parenterally in order to protect the person from a deficiency of this vitamin.

Our experience leads us to believe that if crystalline vitamin B_1 is to be efficacious in any serious nervous disease it must be given in large doses. We recommend the administration of at least 50 to 100 mg. each day, given parenterally in several doses of from 10 to 20 mg. each. It is also our belief that if no response is obtained within a week, further vitamin B_1 therapy will be unavailing. If these dosages result in improvement of the patient, one may be able to carry him along by the oral administration of thiamin, for a complete cure of these diseases takes a long time. A well rounded diet of 4,500 calories should also be given. This diet must be supplemented with vitamin B or with one or more of the following therapeutic agents: dried brewers' yeast (6 ounces [170 Gm.] daily), wheat germ (6 ounces daily) and extract of rice polishings (tikitiki, 3 ounces [85 Gm.] daily).

SPECIFIC NICOTINIC ACID THERAPY

The dietary advice just noted is as applicable to the pellagrin as to patients suffering from the vitamin B_1 deficiencies.

The optimal dosage of nicotinic acid, like that of thiamin, has not been determined. Neither has the minimal dose of nicotinic acid been determined, but it seems to vary from case to case. It is thought that the pellagrin with severe mental symptoms should receive a total of at least 500 mg. per day. This is best administered by mouth in ten equal doses, although it may be administered parenterally. In the extremely severe cases, convalescence may be shortened by the administration of 1,000 mg. daily. We have given as much as 2,000 mg. daily in divided doses without untoward results. There may be some flushing and feeling of warmth in the skin incident to large doses of nicotinic acid.

ABSTRACT OF DISCUSSION

DR. HANS H. REESE, Madison, Wis.: Drs. Aring, Spies and Evans have given a comprehensive clinical survey on the vitamin B deficiencies, based on the experiences of the Cincinnati group. I challenge only the use of the term "neuritis." Wechsler's recommendation to call this neural deficiency a pathologic condition, neuropathy or polyneuropathy should be accepted. The authors stated: "The experimental evidence available tends to show that vitamin B does not play any direct specific role in counteracting the effects of infectious agents"; then again they say: "It is known that the neuritis in certain persons with infectious diseases disappears following the administration of a well balanced diet." I would like to have explained what is considered a well balanced diet for a person with an infectious disease complicated by neuritis. If forty-five million of our population have to exist at present on an annual income of $980 and some four and one-half million on an annual income of $98, it should be made known what a well balanced diet or optimal nutrition for normal physiologic function is which will counteract neuritic complications if members of this group get ill. Furthermore, do

the authors believe that chemical neuritides do not require vitamin B_1, in addition to present-day therapeutic procedures? Since vitamin B_1 is said to be essential for the integrity of the nervous tissue in general, and since its absence may play an important part in the development of neuropathy in a number of nutritional deficiency or metabolic disorders, I would appreciate information as to diagnostic, clinical and laboratory criteria for the assumption of antineuritic B_1 deficiency being present. How is a mild state of pellagra differentiated from a psychoneurotic or psychasthenic state? I cannot do it from the authors' given list of complaints. The section on treatment and general principles of treatment contains such clearly defined, instructive and essential nutritional principles that its contents should be made available to every physician.

DR. J. M. NIELSEN, Los Angeles: In 1932 I had under my care a patient with a severe pellagrinous psychosis. I put him on a high meat diet and in about six months he began to recover his mental capacity. One of his symptoms, which I called a delusion, was that he claimed that his hair was turning black. He had had white hair for about thirty-five years, but after his mental capacity returned he still claimed that his hair was turning black. I examined his scalp and the crown of his head was covered with black hair. Last year I had another patient, aged 86, who had cerebral thromboses and was almost moribund. He took a turn for the better, but his diet had become so deficient that clinical pellagra had developed. I put him on nicotinic acid and nothing else. In a month, black hair was growing on his bald head. About two months ago I put a patient who has no dietary deficiency at all but who had been bald for many years on nicotinic acid, and before I left Los Angeles he had a growth of hair over that bald area about three eighths of an inch long. Now, I should like to ask whether there is any definite experimental or clinical evidence to substantiate the idea that nicotinic acid has some capacity for the production of melanin or darkening, particularly the hair in this area, or whether this is all a coincidence.

DR. GEORGE R. COWGILL, New Haven, Conn.: The question was asked as to the relative importance of protein, fat and carbohydrate, on the one hand, and mineral nutrients, on the other hand, in B_1 avitaminosis. What evidence there is indicates that vitamin B_1 functions primarily in relation to carbohydrate metabolism. About 58 per cent of protein can form sugar in the body. It appears that one should separate the "non-fat calories" from the "fat calories," so to speak, in estimating the human requirement for vitamin B_1. Regarding the minerals, work with the Warburg apparatus in studies of oxidation and reduction involving vitamin B_1 shows that a little manganese in the system is important. There have been some suggestions in the literature that manganese may play some role in the functioning of vitamin B_1 in the body. That is just a suggestion as to how some of these minerals may perhaps come into the picture, although it cannot be said very precisely at the moment how they function. Regarding the quantitative relationship of vitamin B_1 to protein, fat and carbohydrate, I might mention that Dr. Arnold of the University of Wisconsin reported at the recent Toronto meeting of the American Society of Biological Chemists something like 75 micrograms of pure vitamin B_1 as being required for the metabolism of 100 Gm. of protein and carbohydrate; that is to say, the "non-fat calories." That would be a specific contribution in answer to this question. Regarding the effect of cholesterol deficiency, so far as I know cholesterol is not a vitamin. By vitamin I mean a substance which the body needs for its own metabolism and which cannot be made within the organism, hence must be supplied from without. Regarding the man whose gray hair turned black, I might mention that studies have been reported on rats fed a diet lacking the "filtrate factor." When black rats were used for the study and were on the diet lacking the filtrate factor, gray hair developed. When the filtrate factor was later supplied the gray hair became black. Dr. Agnes Fay Morgan of the University of California reported at a recent meeting in Toronto that she had confirmed these observations on brown Boston bull terriers and had produced gray hair in such animals. When the filtrate factor is supplied, the pigment returns. I don't suppose that such experiments explain the appearance of black hair on a human bald head. I think that is perhaps a little bit beyond us at the moment.

DR. RICHARD M. BRICKNER, New York: I would like to ask the authors whether the use of vitamins has brought out any danger symptoms. Are there any cautions to be given in regard to large doses?

DR. CHARLES D. ARING, Cincinnati: In regard to the therapy of the infectious polyneuritides, one rarely sees a case of infectious polyneuritis since the increased interest in nutrition. One does see the neuritis called "Landry's ascending paralysis," or infective neuronitis, or acute infectious polyneuritis. I think it can be stated that no benefit is obtained from vitamin therapy in this disease. In fact, as I noted, progress of neurologic symptoms occurs when the patient is receiving vitamin B_1. Whether or not patients having chemical neuritis improve with B_1 therapy is a moot point. In one case of emetin neuritis in which the dietary had been satisfactory prompt improvement was obtained with intravenous vitamin B_1 therapy. However, other cases of chemical neuritis, such as jamaica ginger paralysis, of which there were a few fresh cases a year or two ago in Cincinnati, did not respond at all to vitamin B_1 therapy. It would be my advice, therefore, that the vitamin be used in these conditions until more information is obtained. As to what constitutes a well balanced diet, it would take too much time to go into this matter, although, as Dr. Reese points out, it is probably the single most important point in this whole discussion. We have described what we think is a well balanced diet in a paper that is to be published. The differential diagnosis between neurasthenia and mild pellagra is a difficult one clinically. As has been said here, the symptoms are similar. There are, however, certain methods of differentiating these conditions. The finding of porphyrins or similar substances in the urine in cases of mild pellagra and the rapid response of the patient to nicotinic acid, which does not occur in the psychoneurotic patient, would make the diagnosis certain. In the differential diagnosis of nutritional neuritis from other types of neuritis, I think probably the most important point would be the history and the progress of the disease. The mechanical, localized types of neuritis are rather simple of diagnosis. Patients who have been exposed to chemicals and other noxious agents usually give the examiner a lead in the history. There are tests such as the Cline method for determining the excretion of thiamin in the urine, which is a procedure not simple enough to be performed in every physician's office. This method of diagnosis is being developed, and there is likely to be a simple chemical method within the near future. One point that might have a bearing on Dr. Nielsen's patients who have grown black hair after the administration of nicotinic acid: Nicotinic acid improves the local circulation in the head and face. In regard to the dangers of overdosage with thiamin or nicotinic acid, there is practically none. We have given as high as 500 mg. of thiamin a day by mouth, and again 500 mg. of thiamin a day intravenously for weeks. We have administered as much as 2,000 mg. of nicotinic acid a day by mouth without any untoward symptoms.

Mitosis.—The usual mechanism of cell division is the rather complicated process of mitosis, but the cells of some tissues (e. g. cartilage cells under certain conditions) are believed to divide occasionally by the simpler method of amitosis, which involves a direct constriction and splitting of the nucleus without any preliminary anatomical changes in the latter. . . . The whole process of mitosis, as seen in tissue cultures, takes from thirty minutes to two or three hours to complete. The duration of mitosis in the living body has been calculated by indirect methods. It has been shown, for example, by correlating the incidence of mitotic figures with the growth rate of regenerating liver, that in this tissue each mitosis lasts on the average forty-nine minutes. There is evidence to show that, under normal conditions of light, there is a twenty-four hourly rhythm in the mitotic division of animal cells, a rhythm which is well known to occur in plants. This periodicity is abolished by continuous exposure to light, but not by continuous darkness. —Clark, W. E. Le Gros: The Tissues of the Body, London, Oxford University Press, 1939.

DEPRESSED SKULL FRACTURES; VALUE OF SURGERY; SEQUELAE

AN EIGHT YEAR FOLLOW-UP STUDY OF NINETY-ONE PATIENTS

MARK ALBERT GLASER, M.D.
AND
FREDERICK P. SHAFER, M.D.
LOS ANGELES

The question of elevation of the depressed fragments in depressed fractures of the skull is one that has been debated for many centuries, and even to this day various opinions are held. It has been assumed that if early elevation is not carried out traumatic cysts, scar formation, adhesions or cerebral softening may occur, which clinically can produce manifestations of psychosis, epilepsy, persistent troublesome and debilitating headache, as well as dizziness.

This series of ninety-one cases has been analyzed for the purpose of determining the disability of the entire group, the sequelae responsible for this disability and the effectiveness of early surgery in the prevention of such symptoms.

This group of ninety-one patients has been divided into five classifications, dependent on the various periods of disability (fig. 1). In group A there are thirty-six patients (39.5 per cent) who were disabled for four months or less. Group B, comprising two patients (2.2 per cent), returned to work at the end of a year. Patients in group C had a permanent partial disability. There were twenty-three patients (25.3 per cent) in this division. Group D was composed of those who were permanently and totally disabled; it consisted of eighteen patients (19.8 per cent). There were twelve patients (13.2 per cent) in group E, all of whom died. Seven of the entire group (7.7 per cent) were women.

This classification indicates that if complaints persist beyond the four months period the opportunity for complete recovery is relatively slight. Approximately 20 per cent of these patients were permanently and totally disabled and 13 per cent died. These results show that, in cases of depressed fracture, permanent disability and mortality are considerably higher than in those cases in which the suffering is from concussion or linear fracture.

In the group of patients who were not unconscious following the original accident or else were only momentarily so affected, all recovered within a period of four months, except two who had brain abscess. In those cases in which there was unconsciousness for from five minutes to twelve hours the difference in time was not associated with any corresponding variation in disability. Thirty-four per cent of the five minute to twelve hour group returned to work within four months, whereas about 54 per cent went on to some form of disability; approximately 11 per cent died. In the twelve to forty-eight hour group 44 per cent died, and a similar proportion went on to partial or total permanent disability. Among those who were unconscious for from two to seven days, about 65 per cent developed permanent disability. It is apparent that the period of unconsciousness is definitely related to disability, and the longer the patient has been unconscious the more chance there is of some form of disability developing. If the patient is not unconscious at all his chances for recovery are extremely good, though there is little difference whether a patient is unconscious for five minutes or for twelve hours. Of the total group of ninety-one patients, 13 per cent were not rendered unconscious following the accident and 9 per cent were only momentarily so affected; 48 per cent suffered from loss of consciousness for from five minutes to twelve hours, 10 per cent from twelve to forty-eight hours and 19 per cent from two to seven days (fig. 5).

As has been previously stated, the purpose of early elevation of depressed fractures has been to prevent development of late symptoms. In this series of cases a correlation of figures 6 and 7 will indicate the results of operative intervention obtained in these cases. In group A, thirty-six patients (39.5 per cent) of the entire series) returned to work within a period of four months or less and have been entirely symptom free up to the present time; twenty-three patients (63.9 per cent) were operated on and thirteen patients (36.1 per cent) were not. This clearly demonstrates that the performance of surgery was not a factor in preventing sequelae, as approximately one third of these patients got along perfectly well without operative intervention. In group B there were two patients (2.2 per cent) of the series; neither was operated on, but they continued to complain of mild headaches and dizziness for a period

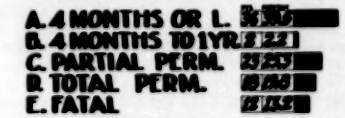


Fig. 1.—Depressed fractures in relation to disability.

of one year. These subjective symptoms then subsided and they were returned to a normal wage earning basis. It is quite evident from these facts that in this group of patients, if complete recovery did not occur within a period of four months, the probability of some form of permanent disability was relatively great. In group C there were twenty-three patients, of whom nineteen, or 82.6 per cent, were operated on. In spite of the fact that the depressions were elevated, these patients developed partial permanent disability. In group D there were eighteen patients, of whom 83.3 per cent were operated on; nevertheless they had total permanent disability. Referring to figure 7, the sequelae may be observed in detail. In addition to these sequelae, the patients complained to a lesser degree of fatigue, insomnia, tinnitus, body pains, transient numbness, staggering gait, anorexia and loss of libido. In group C convulsions occurred in 34.8 per cent of the patients, and in group D in 38.9 per cent. However, in group D extreme psychoses accounted for the disability in 72.2 per cent of the cases, whereas neurologic signs were a minor factor. Subjective complaints of headache, dizziness and nervousness were present in the neighborhood of 50 per cent in both C and D groups but were not necessarily of a disabling nature. All these sequelae except convulsions developed immediately after injury; the psychoses, eliminating the acute psychotic state, of the early part of the injury, showed variations in degree from time to time, while the nervousness frequently increased. The convulsions and psychoses occurred in a much higher proportion than in the series of general

Because of lack of space, this article is abbreviated in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the Section on Preventive and Industrial Medicine and Public Health at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

head injuries.[26] The sequelae in the entire series, groups A, B, C and D, were as follows: headaches 44.3 per cent, dizziness 30.3 per cent, nervousness 27.8 per cent, convulsions 19 per cent, extreme psychoses 16.4 per cent, involvement of the eighth nerve 13.9 per cent, mild psychoses 10.1 per cent, hemiparesis 8.9 per cent,

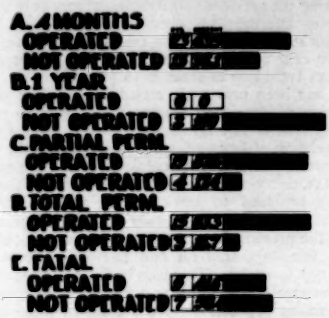


Fig. 6.—Surgery in relation to disability: operations performed, sixty-two (68.2 per cent); operations not performed, twenty-nine (31.8 per cent).

involvement of the third, fourth and sixth nerves 7.5 per cent, aphasia 7.5 per cent, involvement of the first nerve 6.3 per cent and of the second nerve 6.3 per cent.

In forty-one cases in which either partial or total permanent disability developed, the main causes for these disabilities were (fig. 8) convulsions and mental disturbances twenty-four patients (58.8 per cent), convulsions alone fifteen (36.5 per cent), psychoses alone

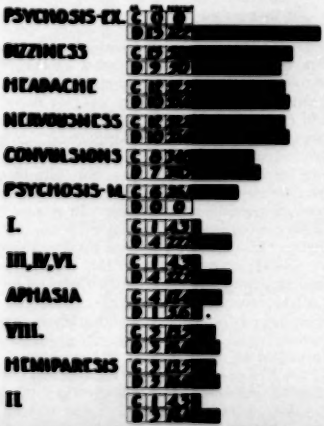


Fig. 7.—Sequelae in relation to disability.

thirteen (31.7 per cent), postconcussion syndrome, aggravated by a mild neurosis in some instances, ten (24.8 per cent), neurologic signs consisting of blindness in three instances and paresis in one (9.8 per cent), and a severe post-traumatic neurosis in three (7.3 per cent).

26. Glaser, M. A., and Shafer, F. P.: Epilepsy Secondary to Head Injury, Arch. Surg. 30: 783 (May) 1935.

The development of a post-traumatic neurosis must not be overlooked in cases of head injury. This may be caused by maladjustments in the emotional realm, financial difficulties, family troubles, antagonism to physician or insurance carrier and dissatisfaction of various and sundry forms.[27] From the industrial standpoint, as well as for the good of the patient, when a post-traumatic neurosis develops and constitutes the main disabling factor present its early recognition is paramount. The cause of the condition must be ascertained and adjusted if possible. Medical care itself is of little avail when finances or antagonism are responsible. In such instances a financial settlement is the best means of solving the problem.

Convulsions occurred in fifteen cases, which is 16 per cent of the entire series. This is a very high percentage of convulsive states following brain trauma as compared to 3.3 per cent reported by us [28] previously in general head injuries. This indicates that depressed skull fractures are exceptionally prone to convulsive states.

Post-traumatic psychosis occurred in thirteen cases to a severe degree and in six cases to a mild degree. In the psychoses there was a complete reversal of personality associated with unreasonable attitude, irresponsibility, unreliability, periodic tantrums or mania. The patients were emotionally unstable, morose, restless

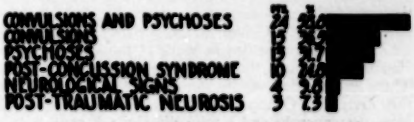


Fig. 8.—Chief causes of permanent disability (forty-one patients).

and unable to adapt themselves to their former occupations. Occasionally this became so severe that they were necessarily confined to a sanatorium. Memory and judgment were often impaired, and restlessness and confusion or moodiness existed.

The abnormalities found on vestibular tests have previously been reported.[29]

SEQUELAE

It is very evident that early elevation did not prevent the development of sequelae in this series; this corresponds to an experimental observation reported by Naffziger and Glaser in 1930.[30] These experiments indicated that the force of the blow struck was responsible for the underlying damage to the brain in simple depressed fractures, and the pathologic condition was not due to a rounded depression of bone pressing on the brain. Elevation should be confined to fractures of a fragmented and spiculated nature wherein the dura has been perforated and the brain traumatized or when the depression is over functioning cortical areas. It is very difficult to lay down a hard and fast rule as to the type of case which does not require elevation, because frequently even by careful radiologic examination we are unable to judge when the dura has been lacerated and the underlying cortex injured. Each case is a problem in itself and requires the personal

27. Glaser, M. A., and Anderson, F. N.: Psychoneuroses Secondary to Head Injuries, Am. J. Surg. 21: 210 (Aug.) 1933.
28. Glaser, M. A., and Shafer, F. P.: Skull and Brain Traumas; Their Sequelae, J. A. M. A. 99: 271 (Jan. 23) 1932.
29. Glaser, M. A.: The Cause of Dizziness in Head Injuries: A Vestibular Test Study in 66 Patients, Ann. Otol., Rhin. & Laryng. 46: 387 (June) 1937.
30. Naffziger, H. C., and Glaser, M. A.: An Experimental Study of the Effects of Depressed Fractures of the Skull, Surg., Gynec. & Obst. 51: 17-30 (July) 1930.

judgment of the surgeon. Immediate elevation is definitely unimportant (figs. 12 and 14). Shock, intracranial pressure, hemorrhage and associated injuries must be considered first. Only when a patient is in good condition is the operation indicated, and it should never be performed without an x-ray examination. The final objective in the operative treatment of a depressed fracture is to renew the depression and repair the cranial defect. When infection is not present the fragments of bone may be replaced. In cases in which a possibility of infection exists, or when the patient has been seen several days after the injury or it is necessary to delay surgery several days, primary wound suture may be carried out as the only immediate operation; then at a later date the depression may be elevated and the bony fragments utilized for repair of the skull. By this means a sterile field is insured for the secondary operation.

The surgeon who favors early elevation in all cases of depressed fracture because he believes that this will prevent the onset of sequelae and is of the opinion that sequelae may be caused by the pressure of bone on the brain should similarly believe that elevation of late fractures is indicated in all instances. This argument could be supported by the theory that continued pressure of bone on the brain will cause further damage and consequently elevation should be carried out at any time with or without symptoms. However, our clinical and experimental data do not justify such conclusions. For this reason we do not favor the early elevation of all depressed fractures, and we definitely do not believe that symptom-free late depressed fractures should be operated on in any instance; further, we

Fig. 9.—Encephalogram of patient with convulsions due to a cyst. Note ventricular changes, cyst and bone defects.

believe that exploration should not be done in cases of cranial defect of long standing and without symptoms for the purpose of preventing later cerebral complaints.

In cases presenting symptoms seen at a late date in which the depression is not elevated, it must be determined whether the symptoms are to be attributed to the injury. In those presenting a post-traumatic neurosis no surgery of any type is performed. In cases of a postconcussion syndrome, with predominating headaches and dizziness, the question of encephalography is seriously contemplated, as it must be remembered that this procedure in many instances relieves the headaches and dizziness.[31] Post-traumatic epilepsy always begins at a late date, and each patient should have an encephalogram performed. Encephalography, plus the use of sedatives in a number of instances, in our

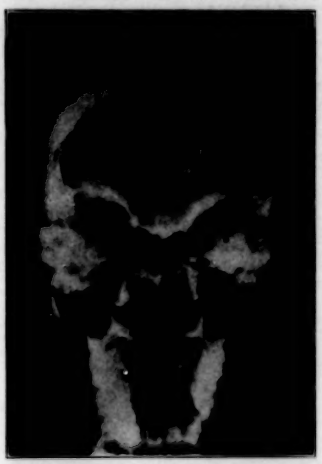


Fig. 10.—Patient with birth injury twenty-four years before suddenly had convulsions. The depressed area is still apparent and the ventricles are dilated, unequal and shifted; cortical air is absent.

series has relieved convulsions, whereas previous to the encephalogram sedatives were not effective. Depending on the encephalographic diagnosis of cysts, adhesions, ventricular distortion or shifts, surgery may or may not be carried out.[32] Little or nothing can be accomplished in the line of surgery for the post-traumatic psychosis. However, an encephalogram will give added information as to the underlying cerebral pathologic condition causing these mental changes. The same type of medical conduct is followed in cases of cranial defects plus symptoms, as in cases in which the bone has not been elevated.

PROCEDURES

A number of methods have been advocated for elevating and removing the depressed portion of bone. In the majority of instances the fragments are badly shattered, depressed and impacted, so that it is quite easy to start the removal of bone by lifting out a single piece, with the aid of a rongeur or elevator. Occasionally it may be necessary to start the elevation by the use of a perforator. All depressed fragments should be removed and the edges of the fracture carefully

31. Carpenter, E. R.: Surgical Treatment of Chronic Headache and Pain in the Head, Southwestern Med. **10**: 61 (Feb.) 1926. Penfield, Wilder: Chronic Meningeal (Post Traumatic) Headache and Its Specific Treatment by Lumbar Air Insufflation, Encephalography, Surg., Gynec. & Obst. **45**: 747 (Dec.) 1927. Gardner, W. J.: The Therapeutic Effects of Encephalography, Pennsylvania M. J. **33**: 126 (Dec.) 1929. Boyd, Douglas: Post-Traumatic Headache Treated by Spinal Insufflation of Air, Arch. Surg. **18**: 1626 (April) 1929.

32. Foerster, O.: Die Pathogenese des epileptischen Krampfanfalles, Deutsche Ztschr. f. Nervenh. **94**: 15, 1926. Penfield, Wilder: Mechanism of Cicatricial Contraction in the Brain, Brain **50**: 499 (Oct.) 1927. Wortis, S. B.: Head Injuries: Effects and Their Appraisal; Experimental Studies of Induced Convulsions and Ventricular Distortion in the Cat, Arch. Neurol & Psychiat. **27**: 775 (April) 1932.

inspected to make certain that any spicules which may have penetrated the dura and injured the brain are not left in situ. By this method the entire underlying dura may be properly inspected and the fragments utilized in the restoration of the skull. The application of a catgut screen for bone replacement will be considered in detail later. The use of an elevator alone,

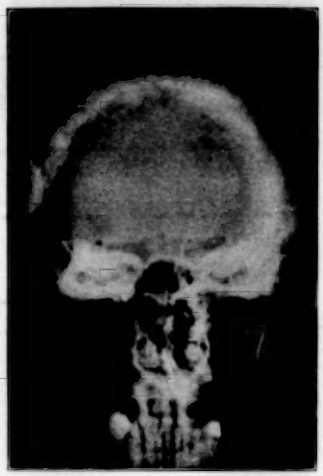


Fig. 12.—Same patient as in figure 11 two years later; note the difference in the depressed portion.

introduced through a small opening with a prying up of the fragments, does not permit inspection of the dura and for this reason is not advisable. It has been suggested that in small depressions a trephine be utilized to remove the entire fragment. The button of bone thus separated may be replaced, thereby elevating the fracture and restoring the bone in one procedure. This method is applicable in only a few instances but proves quite effective when it can be used. In certain instances of compound fracture it has been advised that the area of depression be resected, leaving a wide margin around the broken bone so as to prevent infection of the underlying brain and maintain a sterile field. Since the whole wound is potentially infected in such instances, it is questionable whether asepsis can be maintained. The turning down of a bone flap around the area of depression with the hammering out of the central depressed fragments and replacement of the flap is quite a formidable procedure when restoration can be obtained with more simple means. In addition, the whole principle is defeated should the central bony fragments break away from the bone flap.

The surgery of the dura may be divided into two parts: first, the question of opening the dura when it has not been lacerated and, second, the repair of the dura when it has been lacerated. Peet [7] is of the opinion that the dura should be opened and the underlying brain inspected. It is his belief that the existence of traumatized or devitalized brain has a destructive action on the adjacent normal brain, and by the removal of the devitalized brain tissue the normal brain is protected from further danger and a vicious circle is prevented; softening does not occur, with the result that the brain injury is materially reduced. Gross, Furlow and Sachs do not favor the opening of an uninjured dura. In our own cases we did not open the dura to inspect the underlying brain except when there seemed some probability that hemorrhage or increased pressure was present.

In cases in which the dura was lacerated the traumatized edges were trimmed, and when the dura could be sutured this procedure was carried out. In cases in which the dura cannot be approximated, the question of a dural graft must be considered. Various reasons have been advocated for the use of grafts, and this question at the present time is one of surgical debate. It is believed by some that a dural graft is entirely unnecessary and at times may even be harmful because of a foreign body reaction, which would aid the formation of excessive adhesions. Those who favor the dural graft believe that it is valuable because it prevents the rough edges of the bone from irritating the underlying brain, thus obviating the formation of surface adhesions; also it forms a water-tight closure of the brain and hence opposes the entrance of infection; it hinders or makes impossible the production of a brain fungus should the intracranial pressure rise from any cause, and, finally, since it makes a definite layer over the surface of the brain so as to permit the insertion of bone fragments.[33]

Fig. 13.—Weaving board with catgut woven into a screen.

Experimental studies carried out indicate that the use of a graft just to close the dura is entirely unnecessary since the dura will repair itself, the new cells arising from the edges of the dura and from the overlying fascia and muscle. Should it be necessary to insert a graft, animal membrane has proved just as efficient as an autoplastic graft taken from the fascia lata or the temporal fascia. Further, it has been demonstrated that the heteroplastic graft of animal membrane is entirely absorbed within twelve months, both experimentally and clinically. The use of a dural graft is entirely dependent in each individual case and when utilized is efficient and harmless. All devitalized brain should be removed by dissection and suction, and deeply embedded bone should be extirpated.

It is best to repair the cranial defect immediately at the time of elevation, if this is possible. In wounds

33. Glaser, M. A., and Thienes, C. H.: Dural Defects: How Important Is Their Surgical Repair? California & West. Med. 48:163 (March) 1938.

of a compound nature which are potentially infected, primary suture may facilitate a healing of the wound so that the fragments may be utilized at a later date. The small pieces of bone can be fitted into a mosaic pattern and the entire defect closed. Frequently it is difficult to replace all the fragments of bone and completely cover the defect. It is necessary for all the

Fig. 14.—Particles of bone inserted at time of operation. Note the filling in of defect.

space to be filled with either small particles of bone or bone dust so as to obtain a complete fill of the defect. In order to keep the small fragments in place, a catgut screen may be woven, the catgut sterilized and sutured to the periosteum over the small fragments, thus keeping them in place while the scalp is sutured (fig. 13). This promotes complete ossification of the defect (fig. 14). Cranial defects never fill in, the aperture never grows smaller and the only change that occurs is a smoothing of the sharp borders around the edges of the bone (no infants in series).[34] These defects are closed for cosmetic purposes, as a matter of protection, to remove the psychic effect associated by this absent bone and to prevent the pressure sensations and early morning bulbing, as well as the feeling of cerebral pulsation. The employment of artificial substitutes, such as silver, vulcanite, aluminum, ivory, celluloid and rubber, has been advocated by Elsberg Mitchell, Erdheim and Pringle.[35] The use of heterogenous bone from animals, birds or autopsy material has been suggested by Babcock and Pankratiev. Homoplastic transplants have been taken from the tibia, rib, scapula, ilium and the like (Bagley Breninger, Jones, McWilliams, Primrose, Rhodes, Lexer, Dambrin, Juvara). However, it is the general consensus that osteoperiosteal grafts taken from the adjoining area of the skull are easy to obtain and the results are excellent (Wagner, Frazier, Coleman, Gurdjian, Peet).

In our own series, the osteoperiosteal graft has proved unusually satisfactory. Roentgenograms taken a short time after the graft has been placed reveal the absence of calcium deposit within the graft. However, at a later date islands of bone will become visible, and finally the entire defect gradually becomes smaller, filling in from the edges (fig. 15 and 16). On palpation this area is firm and solid to the touch.

CONCLUSIONS

1. Surgery does not always prevent the development of sequelae because of the existing brain damage associated with the depressed bone.

2. Recovery from depressed fractures occurs without operation in properly selected cases.

3. The sequelae that develop are convulsions, psychoses, headaches, dizziness, nervousness, aphasia, hemiparesis and involvement of the first, second, third, fourth, sixth and eighth cranial nerves.

4. If the patient does not return to work within the first four months, the probability of partial or total permanent disability developing is great.

5. In simple depressed fractures clinical and experimental evidence indicate that the pathologic condition is caused by the original blow struck and not by any irritation of the overlying depressed portion of bone.

6. Injuries resulting from automobile accidents were the most severe; fractures were more frequent in the frontal and parietal bones; fractures in the young and the old were the most serious; 7.7 per cent of the cases were in women.

7. Patients who were not rendered unconscious recovered within four months; those who were unconscious for from five to twelve hours developed approximately the same disability; but, after the twelve hour period, the longer they were unconscious, the greater was the final disability.

8. Early elevation should be confined to fractures of a fragmented or spiculated nature wherein the dura

Fig. 16.—Osteoperiosteal graft inserted. Note closure of the defect three years later.

has been perforated or when the depression is over functioning cortical areas. No hard and fast rule can be laid down for the type of depression to elevate, but, bearing the principles in mind that simple depressions are not harmful, the penetration of the dura cannot always be determined by x-ray examination; personal judgment is essential. Operation should carry no mortality.

34. Glaser, M. A., and Blaine, E. S.: Duration of Fractures and Operative Defects of the Skull (As Revealed by Roentgenograms), J. A. M. A. 107: 21-24 (July 4) 1936.

35. Pringle, J. H.: Treatment of Acquired Defects of the Skull, Brit. M. J. 2: 1105-1107 (Dec. 4) 1937.

9. A badly lacerated wound may be converted into a closed wound by primary suture to conserve the underlying bone and delay early formidable surgery.

10. Patients with late depressed fractures or cranial defects without symptoms should not be operated on.

11. Patients with late depressed fractures or cranial defects, with certain symptoms, should have encephalograms performed and surgery if necessary.

12. Cranial defects never heal spontaneously (no infants in series). At the time of elevation, the use of a catgut screen to hold small fragments of bone in place insures complete ossification of the defect. Late defects are best treated by an osteoperiosteal graft.

ABSTRACT OF DISCUSSION

DR. JOHN H. POWERS, Cooperstown, N. Y.: A number of depressed fractures of the skull are seen in a rural area due almost entirely to the automobile or a kick in the head by an animal. Some of these are exceedingly severe, and three were responsible for deaths in my series of farm accidents. In a rather limited experience I have relied on certain rules in the treatment of depressed fractures of the skull. I feel that any depressed fracture involving both the outer and inner tables overlying the motor area, in which there is even a suspicion of pressure on the dura, should be explored and the fragments elevated. These patients later on are prone to develop sequelae from such depressed fractures over the motor center. Furthermore, I think that every compound fracture of the skull, whether depressed or not, should be operated on, the edges of the wound being extensively debrided and if possible approximated thereafter. If it is impossible to close the wound, it must be allowed to granulate. I was not quite clear as to the relationship of the sequelae, particularly convulsions, in patients operated on and those not operated on. I was particularly interested in the authors' description of the method of treating defects in the skull. I feel that a small defect is of no significance. I am under the impression that in children such small defects may decrease in size over a period of years.

DR. MARK A. GLASER, Los Angeles: In reference to the elevation of a simple nonspiculated depressed fracture of the skull certain fundamental principles must be borne in mind. First, the experimental work has indicated that the blow struck is responsible for the underlying pathologic condition, and not the rounded depression of bone. Second, sequelae developed in 83 per cent of the cases in which operation was performed. While in group A sequelae developed in only 38 per cent of the cases, no operation was performed. From these experimental and clinical results it is evident that fundamentally it is the blow that causes the damage and not the rounded depression of bone and further surgery does not necessarily prevent sequelae. In cases of simple rounded depressed fractures without spiculation or fragmentation of the inner table which would indicate penetration of the dura and over nonfunctional cortical areas we do not favor elevation. Frequently in compound fractures the original wound is sutured and at a later date the bone is handled. In this manner the skull may be conserved without any danger of infection and the fragments replaced so as to prevent a cranial defect. In certain cases in which the question of elevation is a matter of doubt it is always best to carry out the procedure and in all instances the personal judgment of the surgeon in charge is all important. In children when the bones of the skull have become calcified the aperture of the cranial defect does not decrease in size. This has been previously reported by Dr. Blaine and myself. It is true that in children linear fractures may disappear within six months or so whereas in adults they have been found visible as long as seven years later. However, in some instances they have disappeared in eighteen months. The primary treatment of depressed fractures is to consider the brain damage, and the secondary treatment is to restore the skull. When the defects are seen at a late date it is frequently necessary to repair the skull because of the fear of the patients and the subjective symptoms that occur with this defect. In my experience an osteoplastic flap is most satisfactory.

THE REACTION OF THE CORONARY VESSELS TO DRUGS AND OTHER SUBSTANCES

LOUIS N. KATZ, M.D.
AND
ERNA LINDNER, B.S.
CHICAGO

A great deal of confusion exists concerning the reactions of the coronary blood vessels to many products of metabolic origin and to numerous drugs. The prevailing contradictions regarding the reaction of the coronary vessels arise from the circumstances under which the measurements have been made, the indirectness of the methods used in some studies and the abnormality of the conditions in others. We have become concerned with this problem and have developed a method by which the action of various drugs and other substances directly on the smooth muscle of the coronary vessels can be determined without at the same time being altered by the other factors which indirectly affect the rate of coronary flow. Our method, which employs a normal denervated dog's coronary vessels perfused in situ with defibrinated dog's blood, permits a direct determination of whether a substance has a vasodilator or a vasoconstrictor action on the coronary vessels.

It must be emphasized that besides its effect in actively altering the caliber of coronary vessels a drug may also passively change the coronary caliber by its other actions. Hence coronary vasodilatation and coronary vasoconstriction are not necessarily accompanied by the expected changes in coronary flow in the intact animal and in man. Further, for practical purposes the important thing is not whether the substance has a coronary vasodilator or vasoconstrictor action nor whether the substance increases coronary flow or decreases it but rather how it influences the relation of the change in coronary flow to the alteration in the work of the heart and to the energy cost on the part of the heart in doing this work. A drug that dilates the coronary vessels actively and that increases the coronary flow may still be valueless or even harmful if it has a disproportionately greater augmenting action on the energy cost and work of the heart. It is the change in the ratio of coronary caliber and coronary flow to the work and energy expenditure of the heart that is the important criterion in determining the value of a drug.

To evaluate the merit of a drug properly a knowledge of its action (1) on the active coronary caliber changes, (2) on the total coronary flow and (3) on the work and energy expenditure of the heart is necessary. In this report we deal with our results on the first of these factors. Studies are now in progress to determine the effects on the other two.

The passive factors controlling coronary caliber play an important role in determining coronary flow. For example, the pressure fluctuations in the aorta are of prime importance. In estimating their effects it is not enough to know just the mean pressure but also the cyclic alterations between the systolic and diastolic pressures. Likewise we have shown that the pressures existing in the cavities of the heart and the tension developed within the walls of the heart chambers pro-

From the Cardiovascular Department, Michael Reese Hospital.
Read before the Section on Pharmacology and Therapeutics at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.
Aided by the A. D. Nast Fund for Cardiac Research and by grants in aid of the Therapeutic Committee of the American Medical Association and of the National Research Council.

foundly alter the coronary flow.[1] Drugs may produce their action on coronary flow indirectly by affecting these factors rather than by a direct action on the smooth muscles of the coronary vessels, or these side actions may counterbalance the direct action.

Another serious error in measuring coronary flow is the use of the coronary sinus drainage as an index of coronary vasoconstriction or vasodilatation. The coronary sinus is only one of the drainage channels of the coronary system, the others being the thebesian veins, which empty directly into the heart cavities, chiefly on the right side. We have shown[2] that the coronary sinus flow is a variable proportion of the total coronary flow and that therefore it is not a reliable measure of coronary vasoconstriction and vasodilatation. Coronary sinus flow changes may represent alterations in the partition of coronary drainage between it and the thebesian channels rather than the changes in total coronary flow. An idea of the complexities of the factors governing coronary flow may be obtained from the accompanying diagram.

We have recently developed a method of perfusing the dog's coronary system[3] in which the perfusion pressure was maintained constant (at about 120 mm. of mercury) throughout the experiment and in which the intramyocardial tensions and intracardiac pressures were kept constant (at atmospheric pressure) by throwing the ventricles and auricles into fibrillation and keeping the heart cavities open to the outside. We have shown that the incoordinate action of fibrillation is without effect on coronary flow when the heart chambers are open to atmosphere.[4] The coronary flow in our studies was determined by measuring either the total inflow into the coronary arteries or the total coronary outflow leaving the pulmonary artery. In the latter case the error involved in ignoring the thebesian flow into the left heart is negligible.[2] In this preparation, therefore, a decrease or increase in coronary flow, as measured, can result only from an active decrease or increase,

Coronary Vasodilator and Vasoconstrictor Drugs and Substances Based on Observations on the Isolated Fibrillating Dog Heart

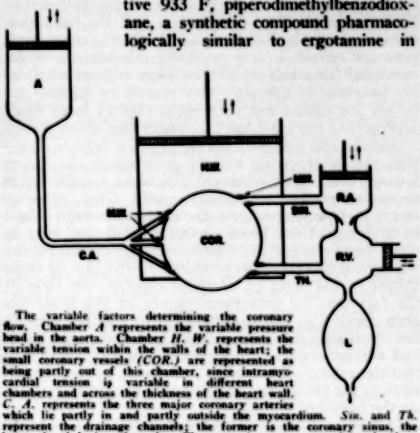
Coronary Vasodilator Drugs and Substances
Epinephrine (at times preceded by mild transitory adrenergic constriction)
Acetylcholine derivatives (cholinergic)
Calcium chloride
Sodium chloride
Potassium chloride (when less than 1½ of normal blood concentration)
Glyceryl trinitrate and sodium nitrite
Histamine
Caffeine, aminophylline and other xanthines
Diffusible substances liberated in myocardial ischemia
Coronary Vasoconstrictor Drugs and Substances
Ergotamine (only at times)
Piperodimethylbenzodioxane
Potassium chloride (when greater than 1½ of normal blood concentration)
Pitressin
Atropine sulfate (mild)
Substance in defibrinated foreign species blood

respectively, in the caliber of the coronary vessel, i. e. vasoconstriction and vasodilatation.

Using this method, we have studied the action of a variety of drugs, salts, bloods of foreign species and temporary coronary ischemia on the tone of the coronary vessels of the dog. The principal effects discussed in this report are summarized in the table.

1. Katz, L. N.; Jochim, K., and Bohning, A.: Am. J. Physiol. **122**: 236 (April) 1938.
2. Katz, L. N.; Jochim, K., and Weinstein, W.: Am. J. Physiol. **122**: 252 (April) 1938.
3. Katz, L. N.; Lindner, E.; Weinstein, W.; Abramson, D. I., and Jochim, K.: Arch. internat. de pharmacodyn. et de thérap. **59**: 399 (Aug. 31) 1938.
4. Katz, L. N., and Lindner, E.: Am. J. Physiol. **124**: 155 (Oct.) 1938.

Epinephrine[5] in all doses used caused the coronaries to dilate, indicating an active diminution in coronary vascular tone. On occasion, transient constriction preceded the dilatation. Ergotamine tartrate occasionally caused constriction but had no effect on the coronary dilatory reaction to epinephrine. The dioxane derivative 933 F, piperodimethylbenzodioxane, a synthetic compound pharmacologically similar to ergotamine in



The variable factors determining the coronary flow. Chamber *A* represents the variable pressure head in the aorta. Chamber *M. W.* represents the variable tension within the walls of the heart; the small coronary vessels *(COR.)* are represented as being partly out of this chamber, since intramyocardial tension is variable in different heart chambers and across the thickness of the heart wall. *C. A.* represents the three major coronary arteries which lie partly in and partly outside the myocardium. *Sin.* and *Th.* represent the drainage channels; the former is the coronary sinus, the latter the thebesian channels. They are shown to empty into chambers *R. A.* and *R. V.*, the right auricle and ventricle respectively; both of these are represented as variable pressure chambers. (For simplicity, the drainage up to 10 per cent by the thebesian channels into the left heart and the considerable thebesian drainage into the right auricle are not shown.) The smooth muscle of the coronary vessels, which represents the site where active vasodilatation and vasoconstriction occur, is indicated by the thickenings *M. W.* *L* represents the pulmonary circuit.

that it inhibits sympathetic vasoconstriction, produced an increase in coronary tone and abolished the preliminary constriction caused by epinephrine, leaving the dilator response of epinephrine unaltered. The increase in coronary flow, definitely established to occur in the normal unanesthetized dog,[5] is probably due to a large extent to this active coronary vasodilatation. Assuming, on the basis of experimental evidence, that the dog is closely representative of the human being in this regard, it would appear that coronary dilatation is the more usual response to epinephrine in man. When constriction does occur, it is probably only a mild preliminary to a more marked and persistent dilatation.

Dilatation was the only effect noted with all doses of either acetylcholine or mecholyl (acetyl-β-methylcholine).[3] The degree of dilatation was dependent on the strength of the dose. Ergotamine and piperodimethylbenzodioxane had no effect on the action of these two drugs. Atropine, however, completely abolished or diminished these responses. Physostigmine, known to accentuate acetylcholine vascular responses elsewhere, antagonized this inhibitory action of atropine. Thus it appears that the initial constricting action of epinephrine and the persistent dilating action of the choline derivatives on the dog's coronary vessels are correspondingly adrenergic and cholinergic, since they are abolished by piperodimethylbenzodioxane and atropine, respectively. This is in accord with our studies on the innervation of the coronary vessels,[6] in

5. Essex, H. E.; Herrick, J. F.; Baldes, E. J., and Mann, F. C.: Am. J. Physiol. **117**: 271 (Oct.) 1936.
6. Katz, L. N., and Jochim, K.: Am. J. Physiol. **126**: 395 (June) 1939.

which, contrary to many investigators, we obtained in this preparation only dilator effects from stimulation of the vagi and both dilator and constrictor effects from stimulation of the sympathetic nerves.

Glyceryl trinitrate (nitroglycerin), sodium nitrite, histamine and caffeine caused marked and persistent coronary dilatation. Some of the other xanthine derivatives (aminophylline, theophylline and the like) produced a similar but weaker effect.[3] On the other hand, pitressin caused a very powerful constriction, which continued for a half an hour or more without appreciably lessening in degree.[3] Our results on digitalis are as yet incomplete but they show that in large doses approaching the toxic level a constricting action occurs.

Sodium and calcium chloride produce definite dilatation, the latter giving a more pronounced and longer lasting effect.[4] Potassium chloride had a variable action depending on the concentration used.[4] Thus, doses up to one and two-thirds times the amount normally found in defibrinated dog blood produced dilatation, whereas doses from one and one-half to two and one-half times the normal concentration produced constriction, at times almost to the point of complete closure. In view of the fact that the potassium content of the blood has been found [7] to increase from 50 to 100 per cent in the circulatory collapse produced by hemorrhage, shock and adrenal cortical insufficiency, it is not improbable that the excess of potassium contributes in these conditions to the circulatory failure by its constricting action on the coronary vessels.

Defibrinated whole blood of sheep, beef and pig caused a marked coronary constriction.[8] This reaction must be due to a coronary constrictor substance in the blood of a foreign species and not, as has been suggested, to histamine, which in the dog causes coronary dilatation.[3] There was a superficial resemblance to an anaphylactoid reaction in that the coronary vessels of the intact animal could be desensitized to this substance by preliminary repeated injections of the same blood in increasing amounts.

We have confirmed the fact that cardiac ischemia leads to a reactive hyperemia in that temporary stoppage of the coronary flow is followed by a noticeable coronary dilatation.[9] The dilatation appears to be due to the destruction of nondiffusible substances or to the accumulation of diffusible metabolites which normally are either nondiffusible or in some way destroyed or modified when oxygen is present. These effects of temporary coronary occlusion suggest that there exists in the heart an efficient mechanism which, by producing coronary dilatation, operates to maintain this organ in a normal state by increasing its blood supply whenever myocardial needs are not met by the existing coronary flow. Such a lack of balance between myocardial needs and coronary blood supply can occur under any one or any combination of the following circumstances: (1) when the blood supplying the heart is of poor quality, (2) when cardiac work suddenly increases out of proportion to coronary flow augmentation, and (3) when there is a primary inadequacy of coronary flow, the result of coronary narrowing or occlusion.

Since the heart is extraordinarily susceptible to relative anoxemia and ischemia [10] and, further, cannot pause for long periods in order to recover from handicaps as can other organs of the body, reactive hyperemia must be viewed as a very important mechanism for maintaining cardiac function. Interestingly, cardiac ischemia, while leading to coronary dilatation, in man often also results in angina pectoris. Because of his pain, the patient is compelled to slacken his activities and hence reduce the work demanded of his heart, thereby tending to bring into closer balance his myocardial needs and blood supply. It is quite probable that coronary vasomotor reflexes and humoral mechanisms may be brought into play to assist this local dilatory compensatory mechanism, but our knowledge concerning this is still far from complete.

The occurrence of powerful constriction in the coronary vessels following ergotamine, piperodimethylbenzodioxane and especially potassium, pitressin and the blood of foreign species suggests the possibility that coronary spasm can and may occur in man. Our results further suggest that under such circumstances calcium may prove of real therapeutic value by decreasing the tone of the coronary arteries. We make the latter suggestion advisedly, however, for, in spite of the consistency with which calcium chloride increased coronary flow in our experiments, this salt is known to augment the strength of the heart beat and also to render the heart, especially when it is depressed, hyperirritable, and thus may lead to ectopic rhythms. Obviously, before calcium can be used therapeutically with safety, evidence must be procured which establishes that its enhancement of cardiac activity is more than compensated for by its coronary vascular action, and the conditions under which its administration becomes hazardous must be more clearly defined.

Following along the line of thought of improving the balance between the work of the heart and the coronary circulation, a few comments regarding the action of epinephrine are pertinent. In spite of the evidence pointing toward improvement of coronary flow, presumably due in large part to active coronary dilatation, angina pectoris in man is known to be precipitated by this drug. It is quite possible that such attacks are the result of a disproportionately greater increase in the work and energy consumption of the heart than in the coronary flow. Coronary sclerosis would, of course, make the disbalance between coronary flow and cardiac work more pronounced.

The analytic method of studying the action of drugs which our experiments exemplify is essential in clarifying the synthetized action of drugs on the various activities of the heart and the circulation in the intact animal. It is vital to rational treatment, but data obtained from such studies must be carefully integrated with the other actions of the drug before the results can be applied in man. This is particularly the case with so-called coronary drugs.

Twenty-Ninth Street and Ellis Avenue.

7. Zwemer, R. L., and Scudder, J.: Am. J. Physiol. **119**: 427 (June) 1937.
8. Katz, L. N.; Weinstein, W., and Jochim, K.: Am. Heart J. **15**: 452 (April) 1938.
9. Katz, L. N., and Lindner, E.: Am. J. Physiol. **126**: 283 (June) 1939.
10. Katz, L. N., and Long, C. N. H.: Proc. Roy Soc., London, s. B **99**: 8, 1925-1926.

ABSTRACT OF DISCUSSION

Dr. Fred M. Smith, Iowa City: I wish to refer to the action of the nitrites and the purine base derivatives and their use in the treatment of coronary artery disease. Even in extensive arteriosclerosis of the coronary arteries the process concerns for the most part the larger vessels, and the smaller arteries, especially the arterioles, are generally remarkably free from involvement. Thus the arterioles and the capillary bed are usually intact and capable of responding to the action of the vasodilator drugs. There does not seem to be any doubt regarding the vasodilating action of the nitrites on the coronary arteries. The results from experimental studies are generally

accepted, and moreover dramatic effects are commonly observed from the use of glyceryl trinitrate and amyl nitrite in the treatment of attacks of angina pectoris. It is believed, however, that the effectiveness of these preparations may be increased if given more often. I usually prescribe glyceryl trinitrate and direct that it be taken three or four times a day in addition to the amount necessary to control attacks, with the idea of possibly promoting the development of collateral circulation. However, one should test out the action of these drugs on the individual. There has been considerable doubt regarding the action of the purine base derivatives. At the present time, however, the evidence is overwhelmingly in favor of a dilating action on the coronary arteries. Furthermore, the clinical results are in general accord with this concept. A fairly good percentage of patients with angina pectoris will derive benefit from these preparations if given in adequate doses. The results, however, are far more striking if a preparation such as aminophyllin is administered intravenously. Dramatic results are commonly observed in the treatment of acute ventricular failure on the left side. Moreover, the pain of acute coronary thrombosis may be abolished by this form of medication.

DR. GEORGE V. LEROY, Chicago: What interested me most was the effect the authors obtained with different drugs on coronary flow and the fact that these results were obtained in denervated, isolated, fibrillating hearts. It has always seemed to me that the denervated, isolated, fibrillating heart does not exactly represent the situation that confronts the therapeutist. He wishes, if possible, to alter the circulation in the coronary arteries to improve the blood flow in terms of a given demand. My experiments have been performed by means of the Morawitz cannula, which the authors do not approve so highly, and, surprisingly, the results are very comparable with theirs. I questioned the validity of experiments even with the cannula, because the dog was under an anesthetic, so I constructed a Rein thermostromuhr, and my experiments with it have paralleled those of Dr. Essex. Using several of the drugs which the authors mentioned, specifically epinephrine and amphetamine, which is related to it, acetylcholine, pitressin, the purine base diuretics and glyceryl trinitrate, I found the variations of the coronary flow to have been in the same direction as when other methods were used. The finding of the same magnitude and direction of flow changes with different methods: with the isolated, fibrillating heart, perfused under constant pressure, the finding of the change of the same magnitude with the Morawitz cannula in the coronary sinus and the finding of the same change in magnitude with the Rein thermostromuhr on a coronary artery of a conscious dog that walks into the laboratory and receives the injection suggest that criticism of any of the three methods in terms of the other is not justified. One point which has interested me was the effect of pitressin. The reduction of flow that the authors found is similar in extent to what I ordinarily find in my preparations, either with the thermostromuhr or with the Morawitz cannula. This restriction in flow may be abolished very promptly by the administration of some of the xanthines. A dose of aminophyllin or theobromine relaxes it completely and the flow comes back to normal. The same is true of amphetamine and epinephrine. It appears that the effect of pitressin is a transitory affair which can be eliminated.

DR. GEORGE K. FENN, Chicago: Dr. Smith called attention to the uniformly good results in the matter of coronary dilation with the purine base diuretics. Our work, in which Dr. LeRoy participated and which was done largely by him, drew pitressin to my attention. Pitressin, measured both by the Morawitz cannula and by the Rein thermostromuhr, caused a tremendous decrease in coronary flow, which we assumed was on the basis of coronary constriction. Because of the widespread use of pitressin as a postoperative medication, we thought that attention might well be drawn to its clinical possibilities. I would hesitate to give a patient who had any sign of coronary disease any considerable amount of pitressin. The same might be said about the potassium salts so often given in shock.

DR. ERWIN E. NELSON, New Orleans: I should like to ask Dr. Katz a question with respect to the action of pitressin versus solution of posterior pituitary. In the laboratory I usually find that pitressin is a great deal more toxic than the equivalent amount of solution of posterior pituitary.

DR. LOUIS N. KATZ, Chicago: We have had no experience with the preparations of solution of posterior pituitary of which Dr. Nelson speaks. I am pleased to know that the results reported by Dr. LeRoy on unanesthetized animals with the Rein thermostromuhr are in accord with data obtained in anesthetized animals with the Morawitz cannula and with the data presented by us on the isolated heart preparation. However, it seems to me that it is hazardous to conclude that the mode of action is identical in the three cases. As we stated in our report, in the intact animal other factors besides active change in the tone of the musculature of the coronary vessels contribute to determine the coronary flow. It is unwarranted, therefore, to attribute all such changes in flow to active coronary dilatation or construction. Only when the role of the passive factors is eliminated or discounted can that deduction be made. For example, histamine decreases coronary vessel tone, as we have shown; yet when it is given to the intact animal or to man the profound drop in blood pressure may counteract this direct coronary action and decrease coronary flow. Again, epinephrine actively dilates the coronary vessels, and this is apparent in the intact animal; yet when given to patients with coronary sclerosis and angina pectoris it will in many instances precipitate an anginal attack because it increases the work of the heart more than it increases coronary flow. I agree with Dr. Fenn that our results point to a hazard in the clinical use of pitressin and large amounts of potassium arising from their marked constrictor action on the coronary vessels. It seems to me just as important to emphasize that calcium is a powerful coronary dilator and that in the form of calcium gluconate it might be judiciously tried clinically when coronary dilatation is needed.

ACUTE OSTEOMYELITIS WITH STAPHYLOCOCCEMIA

A CLINICAL REPORT ON THE USE OF ANTITOXIN IN ITS TREATMENT

LENOX DIAL BAKER, M.D.
DURHAM, N. C.
AND
ALFRED RIVES SHANDS Jr., M.D.
WILMINGTON, DEL.

In 1936 Joyner and Smith[1] reported from Duke Hospital excellent results with the use of staphylococcus antitoxin in the treatment of thirteen[2] cases of osteomyelitis in which staphylococcemia was present. In their series there were eleven survivals and two deaths as compared with eight survivals and eight deaths in their control group of sixteen similar cases in which therapy was identical except for use of antitoxin.

Previously Dolman[3] had reported the results of a series of thirty-two cases of acute staphylococcic osteomyelitis with septicemia which had been treated with staphylococcus antitoxin; in his series there was a mortality rate of 31 per cent. In his control series Dolman, like Joyner and Smith, reported a mortality rate of 50 per cent.

Recently Stookey and Scarpellino[4] stated: "It is remarkable that a vast accumulation of experimental facts pertaining to the protective properties of staphylococcic antitoxin against toxin should produce little clinical interest." We feel that the cause of this lack of clinical interest in the use of staphylococcus antitoxin

From the Orthopaedic Division of Surgery, Duke University School of Medicine.

Read before the Section on Orthopedic Surgery at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.

1. Joyner, A. L., and Smith, D. T.: Acute Staphylococcus Osteomyelitis: The Use of Staphylococcus Antitoxin as Aid to Management of Toxemia and Staphylococcemia, Surg., Gynec. & Obst. 62:1 (July) 1936.
2. Included in sixty-five cases here reported.
3. Dolman, C. E.: Staphylococcus Antitoxin Serum in the Treatment of Acute Staphylococcal Infections and Toxemia, Canad. M. A. J. 31: 1 (July), 130 (Aug.) 1934.
4. Stookey, P. T., and Scarpellino, L. A.: Staphylococcus Septicemia, South. M. J. 32: 173 (Feb.) 1939.

can be explained partly by an inadequate understanding of the criteria of its use and partly by the conflicting results that have been reported by several authors. In reviewing the work of the latter group it is of interest to note that no uniform criteria were followed in the use of the antitoxin, and the other therapeutic measures

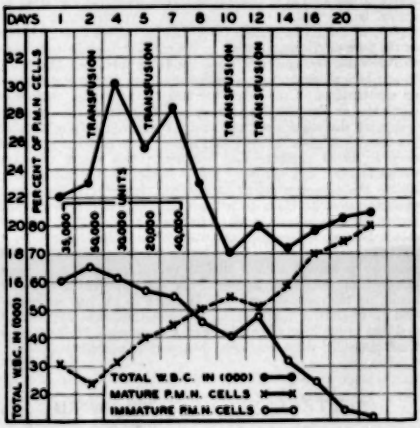


Fig. 1.—Hemogram of a patient with acute staphylococcic disease.

employed were not commensurate with those outlined by Dolman and later by Joyner and Smith.

In 1894 Van de Velde [5] discovered that the staphylococcus produced a filtrable leukocyte-destroying toxin, a leukocidin. Neisser and Wechsberg [6] and numerous other investigators verified Van de Velde's original studies. The observations of these workers have since been expanded by Wadsworth and Hoppe,[7] Burnet,[8] Parker,[9] Pike [10] and others. These investigators have demonstrated a variety of effects of the staphylococcus exotoxin, of which the four most important are (1) the destruction of leukocytes, (2) the hemolysis of red blood cells, (3) the coagulation of plasma and (4) the necrosis of tissue. It has not been established whether these effects are the results of numerous exotoxins or are the result of one exotoxin with a variety of actions. Numerous strains of staphylococci are capable of producing the various effects, and it has been shown by Panton and Valentine,[11] Burky,[12] Dolman [13] and many others that the antitoxin stimulated by one strain of staphylococcus is capable of neutralizing the toxins of any other strains. On this postulate is based the clinical use of the staphylococcus antitoxin. Robertson [14] measured the staphylococcus antitoxin titers in the blood of 305 normal persons and used the titer method in determining the level of antitoxin in the patient's blood. Weaver [15] studied the antitoxin content in well over 200 cases of osteomyelitis and found that in acute osteomyelitis with a favorable prognosis staphylococcus antitoxin appears in unbelievable amounts, whereas in the fatal cases no antitoxin is present.

Joyner and Smith found that the severity of the toxemia in experimental rabbits could be estimated by the shift in the ratio of the mature to the immature polymorphonuclear leukocytes found in the circulating blood rather than by changes in the total white cell count. They found the same to be true in certain patients with acute staphylococcic disease (fig. 1). This decrease in the percentage of mature polymorphonuclear leukocytes was present in the thirteen children with acute osteomyelitis reported by them. In the eleven children of their series who survived, the administration of staphylococcus antitoxin [16] was followed by general improvement, a decrease in the percentage of immature polymorphonuclear cells and an increase in the percentage of mature segmented cells (figs. 1 and 2), whereas in the two children that died the relationship of the mature to the immature cells failed to change following the administration of antitoxin. Stookey and Scarpellino called attention to the hopelessness of cases in which large bacterial emboli lodge in the cortex of the brain or in vital centers inaccessible to surgical drainage. One of their patients who failed to respond to antitoxin therapy died three days after onset of the illness. At necropsy only three small lung abscesses were found, but the viscera were very dark. They interpreted these phenomena as suggesting fixation of the toxin to the tissues. We feel that the latter hypothesis is worthy of further investigation and might well explain the fact that some patients fail to show any response to antitoxin even when apparently adequate drainage has been provided.

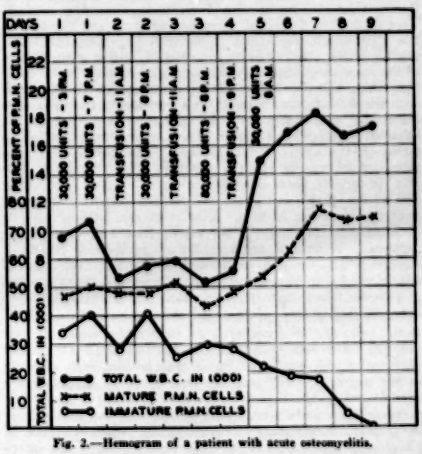


Fig. 2.—Hemogram of a patient with acute osteomyelitis.

As Robertson has pointed out, "Its power to cause serious change in the vascular system is the factor that

5. Van de Velde, H.: Etude sur le mécanisme de la virulence du staphylocoque pyogène, Cellule **10**: 403, 1894.
6. Neisser, M., and Wechsberg, F.: Ueber das Staphylotoxin, Ztschr. f. Hyg. u. Infektionskr. **36**: 299, 1901.
7. Wadsworth, A. B., and Hoppe, E. N.: The Action of Bacterial Culture Products on Phagocytosis, J. Immunology **6**: 399 (Nov.) 1921.
8. Burnet, F. M.: Interactions of Staphylococcus Toxin, Anatoxin and Antitoxin, J. Path. & Bact. **34**: 471-492 (July) 1931.
9. Parker, J. T.: Production of Exotoxin by Certain Strains of Staphylococcus Aureus, J. Exper. Med. **40**: 761-772 (Dec.) 1924.
10. Pike, R. M.: Depression of Phagocytosis by Products of Staphylococci, J. Immunol. **26**: 69-80 (Jan.) 1934.
11. Panton, P. N., and Valentine, F. C. O.: Staphylococcal Toxin, Lancet **1**: 506-508 (March 5) 1932.
12. Burky, E. L.: Studies on Cultures and Broth Filtrates of Staphylococci; Antitoxin Content of Rabbit Serums Immune to Staphylococcus Toxin and Precipitin Reactions of Such Serums, J. Immunol. **25**: 419-437 (Nov.) 1933.
13. Dolman, C. E.: Pathogenic and Antigenic Properties of Staphylococcus Toxin, Canad. Pub. Health J. **23**: 125-132 (March) 1932.
14. Robertson, D. E.: Acute Hematogenous Osteomyelitis, J. Bone & Joint Surg. **20**: 35 (Jan.) 1938.
15. Weaver, J. B., cited by Stookey and Scarpellino.[4]
16. Prepared from the toxin produced by Burky's Ha strain of hemolytic Staphylococcus aureus. Supplied by Lederle Laboratories, Inc.

makes staphylococcal osteomyelitis one of the most dreaded diseases occurring in the young." He is of the opinion that the severity of the disease depends not so much on the number of organisms present as on the individual's natural ability to destroy the organism by phagocytosis and to produce antitoxin to neutralize or render inert the toxins produced by the organism. He reported unsatisfactory results in nine cases of staphylococcic osteomyelitis in which intravenous antitoxin was used. He did not give any review of what criteria he followed in selecting his cases and in administering the serum and he did not give the dosage used except in one case; it is therefore difficult to evaluate his data. There is one important factor which may have influenced his results, that is, his effort to combat the septicemia and toxemia without carrying out early drainage of the site of infection. We are convinced that early drainage is absolutely necessary if one is to combat the constant liberation of toxin from the focus. We have concluded from our autopsy results that a lack of response to antitoxin therapy can in a large percentage of cases be attributed to incomplete drainage of the osteomyelitis or to the presence of inaccessible foci. Robertson's work was not primarily concerned with staphylococcus antitoxin and its use but dealt in detail with staphylococcus titers and toxoids; it is an excellent treatise on this subject and it should stimulate interest in the use of staphylococcus toxoid. Williams[17] has reported the results of the use of staphylococcus antitoxin in the treatment of twenty-four cases of acute osteomyelitis and has compared the clinical course of this series with that of forty-two cases of acute osteomyelitis in which the antitoxin was not used. The size of his doses according to our methods was in the majority of instances entirely inadequate. His cases were evidently picked with no regard to the presence or absence of toxemia. He stated: "Blood cultures, performed in four instances, showed a staphylococcemia" and he concluded that the serum had not been of "much extra benefit"; however, he admitted that little comparison could be made between the potency of his serum and of that used by Dolman. His paper is a comprehensive review of acute osteomyelitis, but it confuses the purpose for which staphylococcus antitoxin should be used. It is not amiss at this time to state that staphylococcus antitoxin has one and only one role: the neutralization of the staphylococcus toxin or toxins which, when liberated in the circulating blood, cause the destruction of leukocytes, the hemolysis of red blood cells, the coagulation of plasma and the necrosis of tissue.

17. Williams, S. W.: The Early Treatment of Acute Staphylococcal Osteomyelitis, M. J. Australia 2: 459 (Sept.) 1937.

TABLE 1.—*Mortality in 103 Cases of Staphylococcemia*

	Total Cases	Survived	Died	Mortality Rate, %
Given antitoxin	47	29	18	38
Not given antitoxin	66	13	53	70
Total	103	42	61	59

STATISTICS

Of 648 cases of staphylococcic disease reviewed in the preparation of this paper there were 103 cases with a definite staphylococcic septicemia; of these 103, in sixty-five there was osteomyelitis. This report is concerned primarily with the cases of osteomyelitis, but the statistics of the 103 cases of staphylococcic septicemia may be of general interest and are therefore recorded (table 1). Of the 103 patients sixty-one died and forty-two survived, a mortality rate over all of 59 per cent. Of the patients not treated with staphylococcus antitoxin forty-three died and thirteen survived, a mortality rate of 76 per cent; whereas of the forty-seven patients treated with staphylococcus antitoxin eighteen died and twenty-nine survived, a mortality rate of 38 per cent. The patients ranged in age from 3 weeks to 66 years; the average age was 20 years. The sixty-five patients with osteomyelitis ranged in age from 3 weeks to 62 years, with an average age of 15 years.

Table 2 shows the age groups of the patients with osteomyelitis and the results for each group. Sixty-five patients with osteomyelitis had proved staphylococcemia. Of these sixty-five there were thirty who did not receive staphylococcus antitoxin; of this group nine survived and twenty-one died, a mortality rate of 70 per cent. There were thirty-five patients treated with antitoxin; of this group twenty-six survived and nine died, a mortality rate of 25.7 per cent. In the group treated with antitoxin the average duration of illness on admission was 7.6 days. In the group not receiving antitoxin the average duration of illness on admission was 9.8 days.

TABLE 2.—*Staphylococcemia with Osteomyelitis*

	Below 5 Years		5 to 9 Years		10 to 15 Years		16 to 20 Years		21 to 30 Years		Over 30 Years		Total			Mortality Rate, %
	Survived	Died	Survived	Died	Survived	Died	Survived	Died	Survived	Died	Survived	Died	Survived	Died	Cases	
Given antitoxin	2	3	10	1	11	3	2	1	..	1	1	..	26	9	35	25.7
Not given antitoxin	..	2	3	2	6	6	..	2	..	2	..	7	9	21	30	70
Total cases	7		16		26		5		3		8		35	30	65	46.1

The blood picture expressed in colonies of staphylococcus per cubic centimeter of blood is shown in table 3. Of the group not receiving antitoxin there were only two survivors whose blood showed over one colony per cubic centimeter and no survivors whose blood showed over ten colonies per cubic centimeter, whereas in the group receiving antitoxin there were eighteen survivors in whose blood there was over one colony per cubic centimeter, and eight of these eighteen showed over ten colonies per cubic centimeter. Of the nine fatal cases in which antitoxin was used, death was attributed to inadequate drainage in five cases, inaccessible foci in two and pneumonia in two. In three of these cases antitoxin therapy was not indicated as each showed a high ratio of mature leukocytes, and in two

TABLE 3.—*Blood Culture in Osteomyelitis*

No. of Colonies per Cc. of Blood	Given Antitoxin		Not Given Antitoxin	
	Survived	Died	Survived	Died
Not recorded	3	..	..	8
1 or less	5	..	7	1
2 to 10	10	1	2	3
11 to 50	4	5	..	2
50 to 100	3	2	..	3
100+	1	1	..	4
Total	26	9	9	21

of the fatal cases there was a favorable response to the antitoxin, that is, there was a shift of the hemogram to the mature side. We feel that in the latter five cases death was due not to the toxic effect of the staphylococcus but to the absorption of nonspecific toxins or to the infection of vital centers.

ROUTINE TREATMENT

As far as possible our routine treatment in suspected cases of osteomyelitis has been carried out according to the following plan but not necessarily in the order named (since the studies are made by several workers, and conditions of course vary in every case): An adequate history is obtained, and a complete physical examination is done. Sedation is carried out as indicated, and the dehydration which is usually present is combated by intravenous fluids in the form of physiologic solution of sodium chloride with 5 to 10 per cent dextrose. A hemoglobin determination is made and red blood cell and white blood cell counts are done. The leukocytes are differentiated to estimate the relative percentage of mature and immature polymorphonuclear cells, and it is on this relationship, regardless of what the total white cell count may be, that we determine whether or not the administration of antitoxin is indicated: antitoxin therapy is instituted if there is an increase in the percentage of nonsegmented and a relative decrease in the percentage of segmented polymorphonuclear cells found in the circulating blood. Blood cultures are planted and the patient is grouped and matched for transfusions; preoperative blood transfusion of from 150 to 200 cc. is given; as a rule, the donor is bled of from 500 to 600 cc. and the remainder of the blood is given in twelve to twenty-four hours or postoperatively. If a diagnosis of osteomyelitis is made, the patient is prepared for immediate operation. The type and extent of operation depend on the individual features of the disease in each case and will be discussed later. It should be said here that immediate and adequate drainage is a prime requisite if the use of staphylococcus antitoxin is to be effective. Preoperative roentgenograms are made as a matter of record but have been of little if any diagnostic value in the earlier cases. Postoperative care will be outlined under the several headings that are to follow. As already stated, we use the hemogram picturing the relative percentage of mature and immature polymorphonuclear cells as the main guide in determining the degree of toxemia which may be neutralized by antitoxin therapy. The general toxemia of the patient, evidenced by high temperature, increased pulse rate, respiratory distress, flushed face, dilated pupils and sometimes delirium, is considered in outlining the general care but not as an indication for the use of staphylococcus antitoxin; the patient might well be neutralizing the staphylococcus toxin with his own antitoxin and his apparent toxic condition be due to other elements. Burnet has pointed out that other factors besides the production of toxin play a part in determining the fatal outcome in staphylococcic infection in animals. Stookey and Scarpellino reported a case in which in their opinion death was caused by the absorption of necrotic products and the nonspecific toxins of necrotic tissue in a surgically accessible area that had not been adequately drained.

TABLE 4.—*Study of Fatal Cases*

	Necropsy	
	Yes	No
Given antitoxin	5	4
Not given antitoxin	13	8
Total	18	12

METHODS OF ADMINISTERING THE SERUM [18]

A skin test for sensitivity should be made intradermally with 0.1 cc. of the undiluted antitoxin; also 0.1 cc. of a 1:10 dilution of normal horse serum should be administered intradermally as a control. Frequently the patient responds negatively to normal horse serum and with an immediate urticarial wheal to the antitoxin. This variation indicates an antigen-antibody reaction in the skin and not a sensitivity to horse serum. Patients showing a reaction to the antitoxin should always receive the first dose intramuscularly, followed four hours later by intravenous antitoxin. As a general rule the first dose of the serum for children under 10 years of age has been 20,000 units administered intramuscularly. Children over 10 have received initial doses up to 40,000 units. If there is no reaction to the first dose, we advocate intravenous administration for the subsequent doses. The antitoxin is administered intravenously with a gravity apparatus. The amount of serum is estimated and twice its volume of saline solution is poured into the gravity apparatus. After the needle is in place, the antitoxin is poured on to the saline solution and administered slowly over a period of twenty minutes or longer. The initial dose is usually followed in four hours by an intravenous dose of from 40,000 to 60,000 units, depending on the size of the patient. The dose of from 40,000 to 60,000 units is repeated after twenty-four hours. Often this is sufficient to shift the white blood cells back to a favorable ratio. If this shift has not occurred in twenty-four hours, from 40,000 to 60,000 units is given intravenously every twenty-four hours until there is a favorable shift.

With the use of the new highly purified serum [19] in the past three years we have had no case of serum sickness. One of our patients, aged 6 years, received 700,000 units and another patient, aged 8 years, received 600,000 units, each within a period of three weeks, and neither developed any sensitivity to the serum.

OPERATION

A detailed discussion of the relative virtues of early or delayed operation in the treatment of osteomyelitis is outside the scope of this paper; however, experience controlled by the results of eighteen necropsies (table 4) has taught us that if antitoxin therapy is to be effective it is necessary that all foci of infection receive early and adequate drainage in order that the constant absorption of the toxins may be eliminated. Our operative procedures vary according to the features of each case: when possible, we follow a modification of the treatment advocated by Orr,[20] that is, free drainage and absolute immobilization. At operation an opening of sufficient size and extent to drain the focus is made. Early in our series we frequently used multiple drill holes as outlined by Starr [21] and have found this procedure satisfactory, but of late we have windowed the bone to assure adequate drainage; we are of the opinion that the results of the latter method are the more

18. The antitoxin used in this series of cases was administered under the direction of Drs. D. T. Smith and W. R. Haas. A more detailed study with the results of antitoxin in the treatment of experimental staphylococcic septicemia will be reported later by these authors.

19. Supplied by Lederle Laboratories, Inc.

20. Orr, H. W.: The Treatment of Early Osteomyelitis by Drainage and Rest, J. Bone & Joint Surg. 9:733 (Oct.) 1927.

21. Starr, C. L.: Acute Hematogenous Osteomyelitis, Arch. Surg. 41: 567 (May) 1922.

satisfactory. It is rare that we find simple incision of a subperiosteal abscess sufficient to provide adequate drainage. In the cases in which this method of treatment was used the acute course has been prolonged and the extent of bony involvement increased. In carrying out the Orr method we deviate somewhat from his original recommendations: we irrigate the incision thoroughly with physiologic solution of sodium chloride but do not apply antiseptics as we feel it is futile to try to kill the infection locally and believe the damage done to the tissues by the antiseptics is detrimental to healing. In making our incision through the periosteum we do not reflect the periosteum but, as suggested by Albee and Patterson,[22] incise round the area to be removed. Before windowing the bone we usually make exploratory drill holes into the suspected area to determine the presence of pus and its exact location. In order better to visualize the type of material coming from the openings, all drill holes are made with the incision filled with ether. After the exact site of infection is determined, the area is windowed or saucerized, depending on the acuteness of the illness. The defect is packed with petrolatum gauze to which an excess of petrolatum has been applied. We use 2 inch gauze with selvaged (finished) edges; we have found this type of material much better than that with the unselvaged edges, as it does not ravel and leave loose threads embedded in the newly formed granulation tissue. The entire wound is filled with the petrolatum gauze and covered by a dry dressing. A plaster cast is then applied to immobilize the part in the optimal position for function. The dressing is not disturbed unless there is a rise in temperature or other signs of increased sepsis. The merits of this type of treatment have been well described by previous writers and need no further discussion here. Convalescent care consists of continued rest and immobilization until healing has taken place or at least until all danger of contracture and deformity has passed. A high vitamin, high caloric diet is augmented by cod liver oil, thiamin chloride and ascorbic acid.

Although our experience in its use is limited, we are of the opinion that staphylococcus toxoid is of definite benefit during the recovery period. Robertson has outlined in detail one method of administering the toxoid. Since the beginning of the preparation of our report Whitby[23] has found sulfapyridine to be an active chemotherapeutic agent in the treatment of staphylococcic infection in mice, and his work has been confirmed by Bliss and her associates.[24] Long[25] noted that the institution of sulfapyridine therapy was followed by a rapid sterilization of the blood in three of five patients ill with staphylococcic bacteremia. He did not report the degree of toxemia or the colony count per cubic centimeter in the blood of the patients treated. He was of the opinion that on the basis of the available experimental and clinical evidence careful therapeutic trials of the drug were warranted. McColl[26] has found sulfapyridine effective in the treatment of staphylococcic infection on the surfaces of the upper respiratory system but has not found the same to be true in undrained areas. Smith[27] has used sulfapyridine in a number of cases treated with antitoxin and, although it is too early to give a final opinion, he states that it appears that the use of this drug in combination with antitoxin may be definitely superior to either treatment when used alone.

22. Albee, F. H., and Patterson, M. B.: The Bacteriophage in Surgery, Ann. Surg. 91: 855 (June) 1930.
23. Whitby, L. E. H.: Chemotherapy of Bacterial Infections (Bradshaw Lecture), Lancet 2: 1095-1102 (Nov.) 1938.
24. Bliss, Eleanor A., and Long, P. H.: Comparative Therapeutic Effects of Sulfapyridine in Experimental Staphylococcus Aureus Infections in Mice, Proc. Soc. Exper. Biol. & Med. 40: 32-34 (Jan.) 1939.
25. Long, P. H.: Sulfapyridine, J. A. M. A. 112: 538-539 (Feb.) 1939.
26. McColl, W. A.: Trans. M. Soc. North Carolina, to be published.
27. Smith, D. T.: Personal communications to the authors.

CONCLUSIONS

1. Staphylococcus toxins can be neutralized in vivo by commercial serum.

2. Antitoxin therapy is indicated only when the patient has failed to create sufficient autogenous antitoxin to neutralize the toxins present.

3. The degree of toxemia can be estimated for clinical guidance by the ratio of the mature to the immature polymorphonuclear leukocytes found in the circulating blood.

4. It is necessary to have early and adequate drainage of all foci of infection if antitoxin therapy is to be effective in combating the toxemia.

5. The antitoxin serum which we have used can be administered intravenously with safety and without the subsequent development of serum sickness.

6. The surgical and postoperative procedures as advocated by Orr in the treatment of acute osteomyelitis have been found to be the most satisfactory as well as the most practical form of surgical therapy.

ABSTRACT OF DISCUSSION

DR. JAMES B. WEAVER, Kansas City, Mo.: For over four years I have measured antitoxin in the blood stream and done Schilling counts, as Drs. Baker and Shands have done, in more than 200 cases of acute, chronic and recurrent osteomyelitis. I get more information from measuring the antitoxin content of the blood stream than I do from the Schilling count. The Schilling count is a much simpler test and is better from that standpoint; however, more things have to happen within the host to produce results and that gives more opportunities for greater error. I have found that in counting 100 cells, which I usually do, there is some variation. To get a really accurate Schilling count one should count several hundred cells. Most of the authors' patients as well as my own in the acute stage received numerous transfusions, and I wonder what the effect of the donor blood had on the Schilling count. The measurement of antitoxin in the blood stream is not foolproof. Theoretically it is not what one would have it, because there are other substances in staphylococcus toxin besides the hemolytic factor, which is the basis of this test. There are leukocythemia and the necrotic element, and this test is based on only one of these. To date it is not known whether these substances run parallel in toxin or not, but by measuring the antitoxin content daily I think I can prognosticate fairly well what is going to happen to the patient. It has been my experience that patients who do not make their own antitoxin do not survive. Those who do make their own antitoxin in a fair amount usually survive but as a rule run into difficulty later on. Their sinuses are much more chronic in healing, and they have much more recurrent osteomyelitis. In cases in which a tremendous amount of antitoxin is produced the prognosis for fairly prompt healing and against recurrence is quite good. As to the mortality in treating these patients with staphylococcus antitoxin, my series is in no way comparable to the authors'. I have never had a patient die of acute osteomyelitis with septicemia to whom I did not give antitoxin. The reason for that was that I was fairly certain that the patient was going to survive and I did not give the antitoxin. Patients who I thought would not survive received antitoxin. So I have a high mortality rate. I have seen positive hemograms, that is, favorable hemograms, as Drs. Baker and Shands show, mounting daily as the antitoxin tide has dropped, so those two factors are not parallel. They are in the first two weeks, but after that not at all.

DR. BEN L. SCHOOLFIELD, Dallas, Texas: I have for some years used an autogenous vaccine in a considerable number of cases of acute and chronic osteomyelitis. That apparently has been of considerable benefit, but when one is doing a great deal of surgery along with it one never knows which does the most

good. Certainly, the vaccines alone cannot be depended on. I tried that on one patient who refused surgery and apparently no particular benefit was obtained, but I do believe that the administration of an autogenous vaccine, made from the patient's own pus, is distinctly beneficial.

DR. LENOX D. BAKER, Durham, N. C.: As to the use of the titer method and the use of white cell counts, at our place the titer method as a clinical procedure is not practical at this time. We find that the white cell count can be followed by clinical clerks and that it is the most practical way we have of judging the amount of toxemia present. As to the value of blood transfusion without the use of antitoxin, all I can say is that our patients who were not given the antitoxin had just as many blood transfusions as the patients who were given the antitoxins. As to the amount of antibodies the donors might carry, we observed a boy aged 16 with osteomyelitis of the femur who had been given sixteen transfusions over a period of thirty-eight days. For the seventeenth transfusion we used an immunized donor; that is, a donor who had been immunized to the patient's own organism. Twenty-four hours after this donor was used the patient's white cell count shifted back to a normal ratio, his temperature dropped to normal and he made an uneventful recovery. I have no doubt that the donor's blood had a great deal to do with it, but we cannot always find such a donor and we do not know which donor will manufacture antitoxin. As to the use of autogenous vaccines, these cases are emergencies that are in need of immediate assistance if recovery is to be hoped for. At this stage vaccines and toxoids have not been of benefit in our hands.

MALE SEX HORMONE

CLINICAL APPLICATION

W. O. THOMPSON, M.D.
AND
N. J HECKEL, M.D.
CHICAGO

The numerous claims and conflicting reports concerning treatment with male sex hormone make it desirable to define its use more precisely.

The testis consists essentially of two parts: (1) the seminiferous tubules, the most important function of which is to produce spermatozoa, and (2) the interstitial cells of Leydig, the most important function of which is to produce male sex hormone.[1] What relationship, if any, exists between these two structures is unknown. On the production of the male sex hormone depends the development of secondary sex characteristics, namely the growth of the penis, scrotum, prostate, seminal vesicles, epididymis, vas deferens, body hair, beard, pitch of the voice and, to some extent, skeletal growth, including the contour of the body. Observations of the last few years have demonstrated conclusively that a delicate balance exists between the anterior lobe of the pituitary and the testis.[2] The pituitary apparently stimulates the activity of the testis, which in turn may serve as a check on the pituitary itself. Various factors involved in the initiation of the pituitary stimulus are not clearly understood. There is some evidence that there may be two gonadotropic factors corresponding to two gonadotropic effects of the anterior lobe of the pituitary. One causes development of the follicles of the ovary and influences the function of the seminiferous tubules in the testis (the so-called follicle stimulating hormone), and the other causes luteinization of follicles in the ovary and influences the activity of the interstitial cells in the testis (the so-called luteinizing hormone). Menopausal and castrate urines contain primarily the follicle stimulating material, while human pregnancy urine contains largely the luteinizing factor and is available under various trade names (follutein, korotron, A. P. L., antuitrin-S). The gonadotropic material from the serum of the pregnant mare (e. g. gonadogen, gamone) and commercial preparations prepared from the pituitary itself contain both factors. It is obvious that the testis may be stimulated selectively.

Two types of hormone therapy are now possible in hypofunction of the testis: (1) stimulation therapy with gonadotropic material and (2) substitution therapy with male sex hormone. With gonadotropic material the testis is stimulated to increased activity so that the testis itself produces more male sex hormone, and it is to be preferred in most instances in which the testis is capable of responding to stimulation. Examples of conditions in which stimulation is indicated are the Fröhlich syndrome, hypopituitarism with secondary hypogenitalism, and undescended testes. In substitution therapy the male sex hormone, which the testis itself is not capable of producing in sufficient quantity when stimulated, is supplied artificially. Examples of conditions in which it is indicated are eunuchism, eunuchoidism and all cases in which the testis is incapable of response because of atrophy or destruction (e. g. the orchitis of mumps). The male sex hormone has also been reported to produce improvement in patients with benign prostatic hypertrophy and to rejuvenate old men. It appears to alter the function of the normal testis as judged by decrease in spermatogenesis during its administration.

In just what form the male sex hormone is secreted by the testis is unknown. The most active substance isolated so far is testosterone, which is six times as potent as androsterone, the first androgenic material isolated from urine. Certain esters of testosterone are much more potent than testosterone itself and in clinical work the propionic acid ester (testosterone propionate [3]) is now most commonly used. In addition to testosterone, which has been isolated from the testis, and androsterone and dehydro-androsterone, which have been isolated from urine, twenty-seven related substances with male hormone characteristics have been prepared synthetically by the degradation of sterols, but these are not used therapeutically. For therapeutic purposes testosterone is made synthetically. It is of the greatest interest that from the ovary, testis and adrenal, which come from about the same location in the embryo, important substances have been isolated which show only slight differences in their chemical structure and which may all be derived biologically from cholesterol (estradiol, progesterone, testosterone, desoxycorticosterone).

Very little androgenic material has been recovered from the urine of young boys and girls from 6 to 10 years of age—only from 0.7 to 2 international units per liter. A marked increase in the amount found in urine begins at about the time of puberty, the urine of an adult male containing from 40 to 100 international units in twenty-four hours.[4] The amount secreted appears

From the Departments of Medicine and Surgery, Rush Medical College of the University of Chicago and the Presbyterian Hospital.

Read before the Section on Pharmacology and Therapeutics at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. There is some evidence that the cells of Sertoli may produce a hormone different from that produced by the interstitial cells.

2. Various factors involved in the interrelation of the pituitary and testes have recently been reviewed by C. R. Moore (Gonadotropic Substances and Male Hormone Effects in the Organism, J. Urol., to be published).

3. The testosterone propionate (oreton) used in this study was supplied by the Schering Corporation.

4. Koch, F. C.: The Male Sex Hormones, Physiol. Rev. 17:153 (April) 1937.

to diminish with advancing years, but no accurate data are available. What role, if any, sex hormones play in embryonic development has not been established, but they may be responsible for the development of secondary sex characteristics. The well marked growth of the interstitial cell mass in the testis of the embryo would suggest this possibility.

For some reason not clearly understood, estrogenic material is found in male urine (the equivalent of 10 micrograms of theelin a day) and female urine is just about as rich a source of male hormone as male urine and contains from 30 to 100 international units in twenty-four hours.[4] Koch has pointed out that human urine is unique in its androgenic content, the urine of the stallion, bull, ram and rat containing but little.

EUNUCHISM AND EUNUCHOIDISM

The value of male sex hormone is shown best by its effect on individuals with complete absence of testicular function, namely castrates and eunuchoid individuals. The persistence of bilateral intra-abdominal cryptorchidism beyond the age of puberty commonly results in a condition similar to that produced by castration early in life. However, eunuchoidism is by no means an inevitable result of bilateral failure of testicular descent. In adults with bilateral intra-abdominal cryptorchidism the interstitial cells may show a surprising degree of function, as judged by the development of a normal size penis and prostate and a considerable amount of pubic hair. When the penis of such a person develops normally the body contour is usually normal, but when genital growth fails to take place a state of eunuchoidism usually results. Eunuchoid individuals are usually tall and often slender with the extremities long in proportion to the trunk. The shoulders and chest are narrow. The voice is high pitched and the person is very shy, effeminate and high strung. There may be a feeble attempt at the production of pubic hair but there is usually little or no axillary hair, no beard and no hair on the chest, abdomen, arms or legs. The genitalia remain infantile. The prostate is usually not palpable. The muscles are small and feminine in type. In striking contrast to patients of the Fröhlich type, they often weigh less than normal and often show no development of breast tissue. Eunuchoidism appears to illustrate the effect of testicular deficiency per se, in contrast to the secondary hypogonadism of the Fröhlich syndrome.

In the treatment of eunuchoidism it is necessary to use large doses of testosterone propionate (from 50 to 100 mg. daily). The doses originally recommended (from 1 to 5 mg. daily) are totally inadequate. During the administration of large doses of this material to eunuchoid individuals the following effects are noted:

1. The gradual appearance of the secondary sex characteristics of the adult male. The infantile penis may become normal in size, the prostate develops, and hair grows in the pubic and axillary regions, on the face and on other parts of the body. The pitch of the voice rapidly assumes its characteristic masculine quality. Erections and seminal emissions become very frequent. Priapism has been described.

2. A marked increase in appetite and body weight (as much as 40 pounds [18 Kg.] in four months). The patients do not become obese but show an enormous increase in the size, firmness and strength of muscles. The material appears to stimulate development of the muscular characteristics of the normal male, whereas in the eunuchoid state the muscle development resembles that of the female. This change is very dramatic.

3. An increase in basal metabolism of as much as 30 points. In our patients who received large doses, the rate was raised above normal.

4. An increase in vigor and sense of well being. The patients are capable of and have the initiative to do much more work, both mental and physical. They seek and become much more proficient in games involving muscle coordination and physical stamina.

5. Loss of their effeminate characteristics. Whereas before treatment they tend to run away from arguments and physical combat, after treatment they tend to welcome opportunities to demonstrate their physical prowess.

Fig. 1.—Appearance of E. W., a eunuchoid patient aged 18, Nov. 11, 1937, before treatment was started. Height 67 inches (170 cm.), weight 111½ pounds (50.5 Kg.).

A typical example of what may be accomplished with this material is shown in the illustrations.[5] As in all conditions involving stimulation, the response is determined not only by the stimulating substance but also by the susceptibility of the organ stimulated. There are thus variations in the amount of growth of the penis that may be produced with large doses. From our observations it would appear that the rate at which the development of secondary sex characteristics can be induced cannot be accelerated beyond a certain point. It is to be remembered that the changes associated with normal puberty occur gradually over a period of several years. The details of treatment in eunuchoid individuals are still to be worked out. It is probably necessary to continue intensive therapy for between one and two years and then continue with maintenance therapy for the rest of the patient's life. What the dose for maintenance will prove to be is unknown. In order to simulate natural phenomena and to prevent the development of the skeletal characteristics of the eunuchoid state, it is probably desirable in cases of bilateral intra-abdominal cryptorchidism to begin treatment just before the age of normal puberty, namely, at about the age of 11 years.

5. Genital growth in eunuchoid persons has been reported by the following:
Hamilton, J. B.: Treatment of Sexual Underdevelopment with Synthetic Male Hormone Substance, Endocrinology **21**: 649 (Sept.) 1937.
Kenyon, A. T.; Sandiford, Irene; Bryan, A. H.; Knowlton, Kathryn, and Koch, F. C.: The Effect of Testosterone Propionate on Nitrogen, Electrolyte, Water and Energy Metabolism in Eunuchoidism, Endocrinology **22**: 135 (Aug.) 1938.
Rubinstein, H. S.: The Induction of Sexual Maturity in the Genitally Hypoplastic Adult Through the Use of Testosterone Propionate, J. A. M. A. **111**: 1818 (Nov. 12) 1938.
McCullagh, E. P.: Treatment of Testicular Deficiency with Testosterone Propionate, J. A. M. A. **112**: 1037 (March 18) 1939.

UNDESCENDED TESTES

In a previous communication to THE JOURNAL we[6] discussed in detail various aspects of the treatment of undescended testis with the anterior pituitary-like principle of pregnancy urine. This material works in cryptorchidism by stimulating the interstitial cells of the testis to produce male sex hormone and produces descent in about one fourth of the cases in young boys. The same results can be produced with male sex hormone itself, but since it may injure the testis it does not appear to be as suitable as stimulation therapy. In rare instances it may cause descent of the testes in eunuchoid individuals. It should be pointed out that both anterior pituitary-like substance and male sex hormone may cause excessive genital growth in young boys and that both may stimulate the rate of skeletal growth. Whether or not this is followed by retardation of growth, so that the final height of the body is reduced, as is the case of some interstitial cell tumors of the testis, is unknown. Both substances are to be used with caution in young boys.

Fig. 2.—Appearance of the patient Dec. 13, 1938, after 629,500 rat units of anterior pituitary-like substance had been given over a period of thirteen months. Height 68¼ inches (174 cm.), weight 112½ pounds (51 Kg.).

FRÖHLICH SYNDROME

In cases of the Fröhlich type the effect of stimulation therapy should be tried before male sex hormone is used. Large doses of gonadotropic factor of pregnancy urine are very effective in this condition. If the testes do not respond to stimulation, large doses of testosterone propionate may be used.

BENIGN PROSTATIC HYPERTROPHY

In contrast to the numerous reports of beneficial results from the use of male sex hormone in benign prostatic hypertrophy, our experience with this material in such cases has been disappointing. Since the male sex hormone causes development of the prostate in the first place, it is not easy to understand how its use in benign prostatic hypertrophy would be beneficial. In twenty-two cases of this disorder, testosterone propionate in daily intramuscular injections produced little improvement in the symptoms and clinical course. No noteworthy reduction in the residual urine occurred. The twenty-two patients fell into two groups. In group 1, made up of nine patients, the average age was 72 years, the youngest patient being 67 and the oldest 91. The prostate gland was enlarged in three cases to grade 3 plus, in four to grade 2 plus and in two to grade 1 plus. Three patients had an average residual urine of from 200 to 500 cc., two of from 100 to 200 cc. and four of less than 100 cc. They were treated from seven to fifty-six weeks, receiving the testosterone propionate in total amounts of from 560 mg. to 3,200 mg. Two patients showed a slight reduction in frequency during the day and two patients experienced temporarily an increase in libido and the frequency of erections, but no noteworthy decrease in residual urine occurred in any of the nine cases. In two cases in this group an acute retention developed during the administration of the hormone. In group 2, made up of thirteen patients, the ages ranged from 58 to 82 years (average 70 years). The prostate was enlarged in one case to 4 plus, in three cases to 3 plus and in nine to 2 plus. In four cases the average residual urine varied from 100 to 200 cc. and in nine it was less than 75 cc. The patients were treated from four to fifty-two weeks, the total amount of testosterone propionate varying from 200 to 3,990 mg. An analysis of the results in this group showed that two patients discontinued treatment because they felt that they were getting worse. In four cases a temporary improvement in erections was noticed; three patients showed a reduction in nocturia; one also noticed a reduction in frequency during the day. The residual urine of the four patients who had more than 75 cc. showed no noteworthy reduction. Conclusions based on smaller quantities than this are not reliable.

Fig. 3.—Appearance of the patient May 4, 1939, after 4,400 mg. of testosterone propionate had been given over a period of four and one-half months. Height 70 inches (178 cm.), weight 147½ (66.9 Kg.). The very slight response to large doses of anterior pituitary-like substance stands out in striking contrast to the marked response to testosterone propionate. Hair, which cannot be seen in the picture, developed all over the body. Note the increase in the size of the muscles, which became stronger and firmer. The prostate, not palpable before the administration of testosterone, became 2 cm. in diameter and bulged into the rectum. There was a marked change in the pitch of the voice. Neither testis was palpable before or after treatment.

Some improvement has been reported from the use of female sex hormone in the treatment of benign prostatic hypertrophy, but these reports are yet to be confirmed with well controlled data.

STERILITY

Since treatment with male sex hormone represents primarily substitution therapy, it does not appear to be indicated in the treatment of male sterility. In fact one of us[7] has been able to depress the number of spermatozoa in men with normal counts almost to the

6. Thompson, W. O., and Heckel, N. J.: Undescended Testes: Present Status of Glandular Treatment, J. A. M. A. 112:397 (Feb. 4) 1939.

7. Heckel, N. J.: Production of Oligospermia in a Man by the Use of Testosterone Propionate, Proc. Soc. Exper. Biol. & Med. 40:658 (April) 1939.

point of azoospermia by the use of testosterone propionate. The spermatozoon count returned to normal after the omission of treatment. In other words, in an individual with normal testicular function it would appear that testosterone propionate produces at least a temporary injury to the seminiferous tubules. These results appear to contraindicate the use of male sex hormone in most cases in which the testes are capable of producing spermatozoa. The problem of sterility is a complicated one and its treatment at present unsatisfactory. In some instances deficiencies in quantity and quality of spermatozoa appear to be related to deficiencies in the function of the anterior lobe of the pituitary. Some improvement in therapy may be expected from the development of a more potent gonadotropic factor from the pituitary. The role of the gonadotropic material from the serum of the pregnant mare in the treatment of sterility in the male is still to be determined. The value of the anterior pituitary-like factor is questionable in sterility because it stimulates primarily the interstitial cells.

THE MALE CLIMACTERIC

There is no definite period of loss of sexual function in the male like the menopause in the female. Nevertheless there does occur some waning of sexual activity with advancing years, the age varying tremendously from person to person. More than 50 per cent of men over 70 years of age are reported to show spermatozoa.[8] Brown-Séquard and others have associated the fatigue and decreased vitality of advancing age with decrease in sexual vigor, and a condition has been described in some males resembling the female climacteric. It is probably true that some men of this type will be helped by male sex hormone,[9] but the details of this form of therapy are still to be worked out.

IMPOTENCE

The promiscuous use of glandular therapy in impotence is to be deplored. Many cases are psychogenic in origin. The first thing is to determine the cause of the impotence. If it is related to a deficiency of testicular function, then improvement may be expected from glandular therapy which may be of the stimulation or substitution type, depending on the capacity of the testes to respond. One man aged 56 was cured of impotence by the administration of the anterior pituitary-like principle from pregnancy urine in a dose of 1,500 rat units three times a week. Until more is known about the possible harmful effects of this type of therapy in old men it is wise to proceed cautiously.

UNTOWARD RESULTS

Three of our eunuchoid patients (from 18 to 26 years of age) receiving large doses of testosterone propionate have shown transitory edema of the ankles, but during the period of edema they felt unusually well and were very anxious to continue with the treatment. One other eunuchoid patient complained that palpitation and tachycardia were so marked that he had to discontinue treatment for a while. Three old men with prostatic hypertrophy had edema of the ankles and shortness of breath during treatment. Thompson[10] reports the development of generalized puffy edema, acne of the face and trunk and precordial pain. In one of his cases precordial pain was so marked that treatment had to be discontinued. In younger men the edema may be caused by retention of sodium and other electrolytes, while in older men it may be caused by cardiac failure resulting from increased activity. The patients who are receiving this material must be followed for a long time to determine whether or not there are any untoward late complications.

SUMMARY

1. Testosterone propionate is an important therapeutic agent.

2. Its administration represents primarily substitution therapy, in contrast to stimulation therapy with gonadotropic material.

3. Its use is indicated in conditions in which the testis is incapable of responding to stimulation.

4. Its most important application is in the treatment of castrate and eunuchoid persons.

5. It may cause a marked reduction in the number of spermatozoa in normal men. For this reason it is contraindicated when the testis is capable of normal function and it is probably of no value in the treatment of sterility.

6. Although it is as effective as the gonadotropic factor of pregnancy urine in undescended testes, treatment with the latter is to be preferred because of possible injury to the testis with male sex hormone.

7. It does not appear to be effective in the treatment of benign prostatic hypertrophy.

8. In the treatment of impotence it is indicated only in those cases in which the natural production of male sex hormone is deficient.

9. Its value in reviving the sexual, mental and physical vigor of old men is still to be determined.

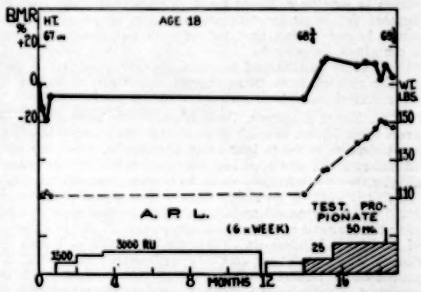


Fig. 4.—Changes in the basal metabolism and weight of the patient during treatment.

ABSTRACT OF DISCUSSION

DR. ELMER L. SEVRINGHAUS, Madison, Wis.: I feel that there is a very definite clinical syndrome which is coming to be appreciated in larger numbers in the last decade or so under the term male climacteric. It has its drawbacks because there is not the same objective evidence of change which the female shows. However, the experience that I have had in a more limited group of cases than that of the authors' indicates that the testosterone is definitely effective in the relief of subjective complaints, more largely of the psychic complaints than of the autonomic and somatic complaints. The testosterone is being used at a time when there is no desire to stimulate or maintain testicular function, and at a time when prostatic hypertrophy

8. Engle, E. T.: Male Reproductive System, chapter 15 in Cowdry, E. V.: Problems of Aging: Biological and Medical Aspects, Baltimore, Williams & Wilkins Company, 1939.

9. Werner, A. A. The Male Climacteric, J. A. M. A. **112**: 1441 (April 15) 1939.

10. Thompson, K. W.: Testosterone for Treatment of the Eunuchoid State, J. Connecticut M. Soc. J. **3**: 59 (Feb.) 1939.

is common. Since testosterone is a material which is known to stimulate prostatic growth, it must be used with some caution until it becomes known whether it is a factor in stimulating the morbid hypertrophies or malignant diseases of the prostate. I wish it were possible for Drs. Thompson and Heckel to tell about the comparative results between the pregnant urine gonadotropic material which they have used so largely and the genuine pituitary gonadotropic materials. I have long felt that the genuine pituitary material would be preferable in those cases in which the objective is the improvement of fertility, the stimulation of the spermatogenic tissues, since spermatogenic tissues show so little or no response to the pregnancy urine material. I wonder if the authors have enough comparative data on the same patient treated with one preparation for an adequate period and then with the other to know whether one of these preparations, pregnancy urine or pituitary material, is superior, judging either by descent of the testes or by the development of the external genitalia. Another question is about the regression of the gains after therapy is stopped. How much of the gain in size of genitalia, how much of the gain in weight, how much of the gain in behavior remains after testosterone is no longer used? Does this require maintained therapy in the treatment of the eunuchoid? There is almost a corollary to that. What should be the objective in treating a eunuchoid? Is there any reason to develop a bigger penis or to develop more hair to increase the frequency with which a man has to shave? It would be my feeling that the only obvious reason to treat a eunuchoid, granting he is permanently infertile, would be if he is socially handicapped or psychologically handicapped and can be relieved from those stigmas sufficiently to become a more normal member of society.

PROF. ERNST LAQUEUR, Amsterdam, Netherlands: It is a great honor for me to speak in your Association and it is also a great pleasure to me to hear about testosterone, which my collaborators and I developed four years ago. We did not expect directly that this substance would have such great clinical value and that it would be so widely known. It is true that the large number of experimental and clinical trials became possible only after the synthetic preparation of testosterone by the procedures of Ruzicka and Butenandt. There are two questions I want to discuss with Dr. Thompson: (1) testosterone and spermatogenesis and (2) testosterone and prostate hypertrophy. 1. It is important if experimental evidence supports the impression in the clinical application of testosterone that with suitable doses the spermatogenesis is improved. In hypophysectomized rats spermatogenesis ceases unless the rat is treated with testosterone propionate, which prevents the loss of spermatogenesis. Clinical cases are reported in the literature and I have had personal experience with two cases in which moderate doses of testosterone restored spermatogenesis and cured sterility. One case of course gives no absolute evidence, but still it shows that spermatogenesis is not interfered with. 2. The treatment of mice with estrogenic substances induces an enlargement of the prostate and ducts of the seminal vesicles and ductus deferens. There are important structural changes (metaplasia of the epithelium, cornification and the like), which remind one of estrous changes in the vagina; de Jongh spoke about "estrus in the prostate." When with the similar treatment the administration of male hormone is combined, the pathologic changes of the prostate are prevented. This is experimental evidence in favor of the effect of male hormones on the prostate. Prostate hypertrophy can also be produced in young dogs by treatment with estrogenic substances. When this treatment is combined with injections of gonadotropic substances, which stimulate the animal's own testis to produce male hormone, hypertrophy of the prostate can be prevented and the naturally occurring hypertrophy in old dogs can so be cured. In 500 human cases I am informed that in more than two thirds some result has been obtained by male hormone. Such statistics may perhaps be considered as evidence in favor of a treatment such as that of hypertrophy of the prostate with male hormone. The lack of positive results in the authors' patients may be due to the fact that these were late cases, treated as outpatients, while clinical treatment was needed.

DR. WILLARD O. THOMPSON, Chicago: As pointed out in the paper, there probably is a condition in certain aging men in which the use of testosterone may be beneficial, not so much because it affects their sexual function as because it increases their mental and physical vigor. But I do think that it is important to proceed cautiously, because the tendency is, once a potent material becomes available, to use it in many conditions in which it is not indicated. Dr. Sevringhaus asked if we had any evidence to suggest whether or not gonadotropic material prepared from the anterior pituitary might be preferable to that from the urine of pregnant women. Theoretically, the pituitary material should be preferable because in patients with hypogonadism one is interested not only in increasing the production of androgenic factor but also in influencing the function of the seminiferous tubules. However, there is no gonadotropic preparation of the anterior pituitary at the present time that is potent enough for routine clinical use, and that was why I said I thought that the pregnancy urine material was to be preferred at present, even though it is far from ideal. Dr. Sevringhaus also asked whether the increase in genital growth showed regression when treatment was omitted. Some regression in the size of the genitalia usually occurs after omission of the anterior pituitary-like principle, the extent varying greatly from patient to patient. In persons of the eunuchoid type, the effect of treatment with androgen is dependent on constant stimulation. While I do not know in detail the effects of omission of treatment, it is probably true that these patients will require some treatment throughout life, because the administration of androgenic substance merely represents substitution therapy. The most important aspect of treatment of the eunuchoid state with androgen is its stimulation of mental and physical vigor and production of a normal psychologic and emotional status. The emotional and psychologic changes in eunuchoid persons are very striking. Dr. Laqueur referred to his very interesting work with androgen which we all know about. He spoke about its being better to use small doses. I must say that we had to use very large doses of this material to produce genital growth in eunuchoid persons. As to the effect of this material on patients with benign prostatic hypertrophy, all I can do is to repeat our results, namely, that we have been unable to obtain any objective evidence of beneficial effect.

MANAGEMENT OF BENIGN STRICTURE OF THE ESOPHAGUS

PORTER P. VINSON, M.D.
RICHMOND, VA.

The frequency with which benign (cicatricial) strictures of the esophagus require dilation has produced the impression among physicians that lesions of this type occur more often than other diseases which cause dysphagia. Contrary to this belief, benign stricture occurs less often than carcinoma and cardiospasm, and with approximately the same frequency as pharyngoesophageal diverticulum. Although benign stricture from swallowing lye is probably encountered less frequently now than prior to legislation requiring that lye be labeled poison, the total number of proved cases of cicatricial stricture has remained practically constant for the past twenty years. Constancy in the incidence of benign stricture has resulted, no doubt, from more accurate recognition of inflammatory lesions in the esophagus in which the cause of inflammation is not known.

Any inflammatory process involving the wall of the esophagus may produce sufficient contraction when healing occurs to reduce the lumen of the esophagus and interfere with passage of food into the stomach. Since formerly one tenth and now one fifth of benign strictures result from idiopathic inflammatory processes and since progressive dysphagia is the only significant symp-

Read before the Section on Gastro-Enterology and Proctology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

tom in this group of cases, it is possible that many lesions which are now recognized as benign were previously considered malignant. Differentiation of benign from malignant stricture may not be possible, and all strictures in the esophagus should be treated as though they were benign unless malignant disease can be proved.

A frequent cause of benign stricture, which was recognized but rarely in the past, is prolonged intermittent ulceration and healing at the junction of the esophagus and stomach that occurs in cases of so-called congenital shortening of the esophagus with hernia of a portion of the stomach through the esophageal hiatus in the diaphragm. Many such cases have been reported as peptic ulcer of the esophagus with formation of stricture.

Stricture from a simple inflammatory process that involves the wall of the esophagus is single and usually located in the lower portion of the organ. When a caustic is swallowed, the lumen of the entire esophagus may become stenosed or there may be single or multiple areas of narrowing. Frequently one of the strictures is in the upper portion of the esophagus. Superficial areas of esophagitis rarely produce sufficient scarring to reduce the lumen of the esophagus and interfere with deglutition. When inflammation involves the muscular layers of the esophagus, contraction occurs and dysphagia follows.

Difficulty in swallowing depends as much on reduction of elasticity of the wall of the esophagus as on actual narrowing of the lumen of the tube. This fact explains the severity of dysphagia in carcinoma when the lumen through the esophagus is fairly large, but elasticity of the wall of the esophagus is greatly reduced, as contrasted with relatively easy deglutition in benign stricture when the lumen is small but the wall more elastic. Infiltration of the muscular layers of the esophagus in carcinoma reduces elasticity of the tube and causes difficulty in swallowing, whereas a patient who has a carcinomatous growth in the esophagus without involvement of the muscular coats may experience little or no difficulty with deglutition. Multiple areas of narrowing in the esophagus may not be associated with a greater degree of dysphagia than is observed in cases in which there is a single stricture.

In burns of the esophagus from ingestion of strong inorganic acid and solutions of lye or ammonia, the severity of the burn is usually dependent on the concentration and amount of solution that has been swallowed. Although this is not always true and severe extensive stricture may follow ingestion of a small amount of caustic, yet patients who have intentionally swallowed a large amount of a concentrated solution of acid or alkali usually have multiple areas of stenosis of the esophagus, if they survive.

One must remember that strictures may occur in the stomach when a large amount of caustic, acid or formaldehyde has been swallowed. Formaldehyde rarely, if ever, produces serious erosion of the esophagus but, when retained in the stomach, it may cause extensive ulceration. In order that strictures in the stomach and especially at the pylorus may not be overlooked, roentgenoscopic examination of the stomach should be made of all patients who have swallowed a large amount of a corrosive substance. In most cases roentgenoscopic study should be deferred until the lumen of the esophagus has been dilated sufficiently to permit free deglutition.

Sodium or potassium hydroxide in granular form is rarely introduced into the mouth except accidentally. It is seldom swallowed, and burns from it are usually limited to the mouth and lips. Stricture of the mouth may occur following burns of the lips and may require plastic operation. Immediate treatment of an injury of this type consists of removal of as much of the caustic as possible with water and application of olive oil to the burned surface.

When a solution of lye has been swallowed, a large amount of olive oil should be given by mouth and supportive measures should be instituted. It is questionable whether attempts should be made to wash the stomach, because introduction of a stomach tube is associated with trauma. Daily introduction of rubber tubes of increasing size immediately following ingestion of a caustic has been advocated to prevent formation of stricture, but I have not had any experience with this type of treatment. When acid has been swallowed, administration of magnesium hydroxide as an antidote is preferable to sodium bicarbonate.

Regardless of the type of chemical that has been ingested, pain and swelling usually prevent deglutition for three or four days. During this period an adequate amount of fluid should be administered by various routes, especially intravenously. As soon as the immediate inflammatory reaction has subsided, fluid can be taken by mouth, and within a week the patient is usually able to swallow soft food.

As healing progresses, the lumen of the esophagus decreases in size, and within a month or six weeks' contraction of scar tissue may become so pronounced that there is complete symptomatic obstruction. If the patient is permitted to reach this stage of dysphagia without having swallowed a thread, gastrostomy may be considered necessary. If, however, a size D twisted silk thread has been swallowed as soon as the initial reaction of the burn has subsided, dilation may be performed when necessary without subjecting the patient to the risk, discomfort and expense of gastrostomy.

When a patient has ingested even a small amount of acid or caustic, a thread should be swallowed and kept in the esophagus until treatment by dilation is required or until it has been determined that a stricture is not present. When the patient is a small child, it is advisable to introduce the thread through a nostril or to withdraw it through the nose after a yard or more has been swallowed, so that the child cannot sever or fray the thread with his teeth.

Even when a patient seems to have complete closure of the esophagus and gastrostomy appears necessary, effort should be made to introduce a thread through the esophagus while fluid is administered preparatory to operation. In most cases a thread will pass through the esophagus although obstruction may seem to be complete, and, as soon as a thread has entered the stomach, fluid can be swallowed. The thread seems to promote passage of fluid through the esophagus just as a urethral filiform bougie facilitates passage of urine through a urethral stricture.

Gastrostomy is associated with a mortality rate of at least 10 per cent and requires hospitalization for ten days or longer. It adds to a patient's discomfort and should seldom be required if a swallowed silk thread is utilized in treatment. Another disadvantage of gastrostomy which is rarely emphasized is that the esophagus may close completely after a tube is introduced into the stomach and the immediate emergency is mitigated. Closure can be averted by having the patient swallow a thread and allowing it to remain in the lumen of the stricture until dilation can be performed. How-

ever, even though this precaution is not observed, complete anatomic stenosis of the esophagus seldom occurs. Recently I observed a patient with cicatricial stricture of the esophagus following ingestion of hydrochloric acid, who had had complete symptomatic occlusion for eight years. Even after this length of time the patient was able to swallow a thread, and normal deglutition has been restored. Gradual dilation of benign stricture of the esophagus with metal sounds will eventually result in restoration of normal swallowing.

Almost all strictures can be dilated to size 30 French at the first treatment, and the size can be gradually increased to 45 French. Not more than one sound should be passed through the esophagus at each treatment, and the interval between dilations and the size of the dilators should be gradually increased. It is advisable to pass dilators from above downward, even when gastrostomy has been performed and the thread has been withdrawn from the abdominal opening. Passage of large dilators from below upward is attended with greater discomfort and the abdominal wound is subjected to unnecessary trauma.

Appearance of patient mentioned in text, for whom normal deglutition has been restored following complete symptomatic obstruction of esophagus for eight years.

Esophagoscopy is not necessary in the management of the majority of cases in which there is a benign stricture of the esophagus. Direct inspection of the esophagus is desirable for patients with strictures which may be benign, when the etiology is uncertain, or in instances in which sudden complete obstruction may have resulted from impaction of a foreign body within the lumen of the stricture. However, dilation of strictures through an esophagoscope is attended with greater discomfort and risk than when dilators are passed into the stomach over a guiding thread. If gastrostomy is contemplated and the patient has difficulty swallowing a thread, esophagoscopic examination should be performed to ascertain whether or not the opening through the stricture is sufficiently large to permit passage of a small ureteral catheter which may be used as a guide for introducing dilating sounds into the stomach.

I have not had any experience with the use of heated bougies as suggested by Dean. Cutting of strictures by various methods is associated with unnecessary risk and discomfort. Impermeable stricture of the esophagus is seldom encountered, but, when anatomic stenosis exists, attempts to restore the lumen of the esophagus almost always result fatally. It is my belief that, when the lumen of the esophagus has been obliterated, establishment of an opening through the scarred tissue is impossible. Reconstruction of the esophagus because of benign stricture has been accomplished in a few cases, but the risk of operation is great and the functional result has not been entirely satisfactory.

SUMMARY

1. Benign stricture of the esophagus occurs less frequently than carcinoma or cardiospasm.

2. In 20 per cent of cases in which there is stricture of the esophagus the cause cannot be ascertained. In these cases carcinoma is usually suspected, and accurate diagnosis may not be possible even following esophagoscopic examination and removal of tissue for microscopic study. Unless carcinoma can be proved, stricture of the esophagus should be considered benign.

3. Congenital shortening of the esophagus with herniation of a portion of the stomach through the diaphragm is frequently associated with stricture at the junction of the esophagus and stomach.

4. When a thread is employed as a guide for passing sounds, a benign stricture can be dilated with a minimal amount of risk and discomfort and with an excellent functional result.

5. Complete anatomic stenosis of the esophagus rarely occurs and can always be prevented by having the patient swallow a thread and allowing it to remain within the lumen of the esophagus until dilation has been accomplished. A patient was able to swallow a thread after having obstruction of the esophagus for eight years. Normal deglutition was restored by gradual dilation of the areas of stenosis.

6. Gastrostomy is seldom necessary in the management of benign stricture of the esophagus and adds to the risk of treatment.

7. In order that stricture at the pylorus may not be overlooked, roentgenoscopic examination of the stomach should be made of all patients who have swallowed a large amount of a corrosive substance. Roentgenoscopic study should be deferred, however, until after the lumen of the esophagus has been restored by the passage of sounds.

300 Medical Arts Building.

ABSTRACT OF DISCUSSION

DR. JOHN H. FITZGIBBON, Portland, Ore.: Important advances in medicine are usually based on simple principles, and I feel that the introduction of the silk thread as a guide in the treatment of stenosis of the esophagus was one of the truly great advances. Regardless of the type of dilator used, the silk thread guide has made the passage of instruments a comparatively safe procedure in experienced hands and has saved patients much unnecessary discomfort and risk. I generally use the metal olive type of dilator originated by the late Dr. B. W. Sippy, because I believe that the piano wire guide, passed over the original silk thread guide, renders the procedure somewhat more safe than the thread alone. However, any one doing this work must be prepared to vary his technic at times, owing to individual peculiarities of the case and sometimes to devise modifications of existing instruments or to originate instruments adapted to immediate needs. Dr. Vinson's reminder that benign stenosis of the esophagus is not infrequently caused by conditions other than the swallowing of corrosives deserves attention particularly since congenital shortening of the esophagus is still frequently misdiagnosed. Legislation requiring that preparations containing lye bear a "poison" label has surely reduced the incidence of lesions due to the accidental swallowing of such corrosives. However, such labels have at times led to the taking of lye preparations with suicidal intent. This spring I observed two patients who swallowed drano, an effervescent lye mixture used for cleaning out drain pipes. The author has emphasized the fact that

gastrostomy is seldom necessary in cases of corrosion if a thread is swallowed early, and I wish to mention the desirability of early and adequate dilation, especially in children. I have had experience with a few children who were allowed to struggle along on liquids and an inadequate diet for several years, with resultant evidence of developmental deficiency, seen particularly in the teeth. I agree with Dr. Vinson that esophagoscopy is usually not necessary in the management of patients with benign stricture of the esophagus unless there is doubt as to diagnosis or possibility of impaction of a foreign body. Certainly, treatment with a dilating instrument passed over a thread or a piano wire guide is much less uncomfortable and continues to give splendid results with reasonable safety.

RESPIRATORY ALKALOSIS DURING ANESTHESIA

AN EXPERIMENTAL STUDY IN MAN

M. H. SEEVERS, PH.D., M.D.
R. T. STORMONT, PH.D.
H. R. HATHAWAY, M.D.
AND
R. M. WATERS, M.D.
MADISON, WIS.

Increased pulmonary ventilation in the human individual, whether voluntary or involuntary, is accompanied by a series of biochemical and physiologic changes which are proportional to the intensity and duration of hyperventilation. The resulting symptoms and signs are numerous,[1] but certain of these are reasonably characteristic. Dizziness, blurring of vision, and numbness and tingling of the extremities are frequent early symptoms. Excessive pulmonary ventilation, long continued, results usually in spasms of the muscles of the face, hands and feet. In some persons these signs are accompanied or followed by laryngeal stridor, opisthotonos, generalized convulsions and unconsciousness. Physical and nervous fatigue are common sequels to the episode and may persist for several days.

The exact biochemical basis for these changes in the irritability of nerve cells has not been clearly established. It is probable that some of the symptoms and signs are initiated by the train of events which follow local restrictions in blood flow secondary to the alkalosis. Schneider [2] and Collier, Densham and Wells,[3] among others, have demonstrated a marked peripheral constriction, and it is not unreasonable to believe that a similar constriction may occur in cerebral vessels, since they are known to respond readily to chemical alterations in the blood.

It is apparent from the literature that the integrity of the cardiovascular system as a whole is maintained even during severe respiratory alkalosis. Norlin [4] has established that the cardiac output, the pulse rate and the consumption of oxygen increase in proportion to the intensity of hyperventilation. Although Henderson, Prince and Haggard [5] observed a fall in venous pressure in short experiments, this has not been confirmed by Schneider,[2] who obtained an increase in both capillary and venous pressure. Arterial pressure changes are insignificant. A slight rise or a slight fall may accompany voluntary hyperpnea [6] or those clinical states associated with hyperventilation.[7] We have failed to find a description of cardiovascular changes associated with hyperventilation in man which might be rightfully termed shock, according to the modern definition or usage of this term.

Until recently these relatively minor and seemingly compensable effects of respiratory alkalosis on the cardiovascular system of man were difficult to harmonize with the more profound changes which are observed in the anesthetized animal when the latter is subjected to excessive pulmonary ventilation. Henderson [8] was the first to describe experiments in which circulatory failure and "fatal apnea" resulted from hyperventilation of the anesthetized dog. These observations served as the basis for his well known theory of acapnial shock. Numerous investigators [9] have observed the arterial hypotension which he described, but there is no uniformity of fact or opinion regarding the significance of this phenomenon or its relation to shock.

It is now clear that the observed differences in the circulatory response of man and animal were more apparent than real, since recent laboratory studies [10] in the dog in which the maximum pulmonary ventilation compatible with the structural integrity of the lung was maintained for from one to fifteen hours established the fact that "acapnial shock," so called, is a phenomenon of narcosis. Furthermore, the changes in the circulation observed in the anesthetized dog cannot rightfully be termed shock when measured by the accepted standards for this condition, since the arterial hypotension is not progressive and does not significantly affect survival even though the condition may exist for many hours. It is evident that in some of the previously reported experiments trauma must have

Supported by the Wisconsin Alumni Research Foundation and the Squibb Research Fund.
From the Departments of Pharmacology and Anesthesia, University of Wisconsin Medical School.
The authors were given valuable assistance by Drs. W. H. Cassels, T. Gordh, M. D. Leigh and H. C. Slocum.
Because of lack of space, this article is abbreviated in THE JOURNAL. The complete article appears in the authors' reprints.
Read before the Section on Miscellaneous Topics, Session on Anesthesia, at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. Harwood, R.: Hyperventilation Tetany, New England J. Med. **218**: 602 (April 7) 1938.
2. Schneider, E. C.: A Study of the Respiratory and Circulatory Responses to a Voluntary Gradual Forcing of Respiration, Am. J. Physiol. **91**: 390 (Jan.) 1930.
3. Collier, R. J.; Densham, H. B., and Wells, H. M.: The Influence of Respiratory Movements on the Cutaneous Circulation, Quart. J. Exper. Physiol. **18**: 291 (Dec.) 1927.
4. Norlin, G.: Circulation and Forced Respiration in Man, Skand. Arch. f. Physiol. **64**: 239, 1932.
5. Henderson, Yandell; Prince, A. L., and Haggard, H. W.: The Influence of Forced Breathing on the Circulation, J. Pharmacol. & Exper. Therap. **11**: 203 (April) 1918.
6. Schneider,[2] Collier, Densham and Wells,[3] Norlin,[4] Henderson, Prince and Haggard.[5]
7. Kerr, W. J.; Dalton, J. W., and Gliebe, P. A.: Some Physical Phenomena Associated with the Anxiety States and Their Relation to Hyperventilation, Ann. Int. Med. **11**: 961 (Dec.) 1937. Harwood.[1]
8. Henderson, Yandell: The Cause and Phenomena of Surgical Shock (Probably Due to a Diminished CO_2 Content of the Blood), Proc. Am. Physiol. Soc., December 1905; Am. J. Physiol. **15**: 28 (Proc.) 1906; Acapnia as a Factor in Shock, Brit. M. J. **2**: 1812, 1906; Acapnia and Shock: IV. Fatal Apnea After Excessive Respiration, Am. J. Physiol. **25**: 310, 1910; Acapnia and Shock: VII. Failure of the Circulation, ibid. **27**: 152, 1910.
9. These include:
Janeway, H. H., and Ewing, E. M.: The Nature of Shock: Its Relation to Acapnia and to Changes in the Circulation of the Blood and to Exhaustion of the Nerve Centers, Ann. Surg. **59**: 138, 1914.
Dale, H. H., and Evans, C. L.: Effects on the Circulation of Changes in the Carbon Dioxide Content of the Blood, J. Physiol. **56**: 125 (May) 1922.
Campbell, J. A.: Carbon Dioxide Tension and Oxygen Consumption During Artificial Respiration, Acidosis and Alkalosis, J. Physiol. **57**: 386 (Aug.) 1923.
McDowall, R. J. S.: The Effect of Carbon Dioxide on the Circulation: Part I, J. Physiol. **70**: 301 (Oct.) 1930.
Shaw, L. A., and Messer, A. C.: Transfer of HCO_3 Between Blood and Tissues Caused by Alterations of CO_2 Concentration in Lungs, Am. J. Physiol. **100**: 122 (March) 1932.
Roome, N. W.: The Cardiac Output in Hyperventilation by External Alternating Pressures, Am. J. Physiol. **104**: 142 (April) 1933.
10. Seevers, M. H.; Stormont, R. T.; Hathaway, H. R.; Orcutt, F. S., and Shideman, F. E.: Acapnia and Shock, J. Pharmacol. & Exper. Therap. **60**: 117 (June) 1937. Stormont, R. T., and Seevers, M. H.: The O_2 and CO_2 Tension in Tissues Following Prolonged Hyperventilation, Am. J. Physiol. **119**: 410 (July) 1937. Seevers, M. H., and Stormont, R. T.: The Relation of Anesthesia to Acapnial Hypotension, J. Pharmacol. & Exper. Therap. **66**: 31 (May) 1939. A series of papers by these authors in press, J. Pharmacol. & Exper. Therap.

played an important role. The evidence on which these statements are based is as follows:

No significant fall in the arterial pressure (greater than a few millimeters) occurs during excessive mechanical hyperventilation in the unanesthetized dog or during the recovery period from cyclopropane or pentothal anesthesia. The dog is therefore not basically different from man in its response to hyperventilation.

A decrease in arterial pressure, which varies from 10 to 50 per cent of the initial level, almost invariably occurs in the anesthetized dog during hyperventilation irrespective of the type of narcotic used. Furthermore, the degree of arterial hypotension is proportional to the depth of narcosis rather than to the magnitude of pulmonary ventilation. A gradual recovery of arterial pressure occurs during prolonged hyperventilation in the anesthetized dog, so that the original or a greater level is attained after several hours. Fatal circulatory failure during hyperventilation occurred only once in eighty dogs, this animal having a chronically enlarged heart with numerous mitral vegetations. Fatal respiratory failure did not occur in a single animal in this series unless ventilation was so severe as to result in rupture of the lung or in those experiments in which a large quantity of narcotic was purposefully administered just prior to the discontinuance of hyperventilation. Arterial hypotension is not observed in the anesthetized dog during hyperventilation if rise in plasma pH is prevented by gastric perfusion of 0.25 per cent hydrochloric acid, even though arterial carbon dioxide tension may be reduced to 5 mm. of mercury. Anesthetized dogs permanently survive from six to eight hours of the most severe hyperventilation. Hyperventilation tetany does not occur in the anesthetized dog.

Since these experiments establish the fact that narcosis modifies significantly the cardiovascular and respiratory response to respiratory alkalosis in the dog,

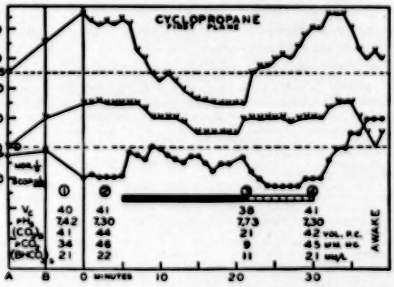


Chart 1.—Hyperventilation with oxygen during cyclopropane anesthesia. *S*, systolic, *D*, diastolic arterial pressures; *P*, pulse; solid block, hyperventilation; block with bars, apnea in minutes; encircled numbers, capillary blood samples; V_c, cell volume per cent; pH_a, plasma pH; $(CO_2)_b$, whole blood carbon dioxide content, volumes per cent; pCO_2, carbon dioxide tension, millimeters of mercury; $(BHCO_3)_a$, base bicarbonate, millimols per liter of plasma.

it becomes pertinent to know whether such is the case in man. We have been unable to find any publications dealing with an experimental approach to this problem, although many of the functional disturbances which occur during or following anesthesia, e. g. circulatory failure and "fatal apnea," [11] atelectasis and pneumonia [12] and "ether spasm," [13] have been gratuitously ascribed to a reduction in carbon dioxide.

Whereas the large majority of all clinical administrations of narcotic drugs are associated with a respiratory acidosis from hypoventilation and the resulting carbon dioxide retention, there are certain circumstances in which hyperventilation may obtain. "Controlled respiration" is now a rather common practice of professional anesthetists. The tendency of novices

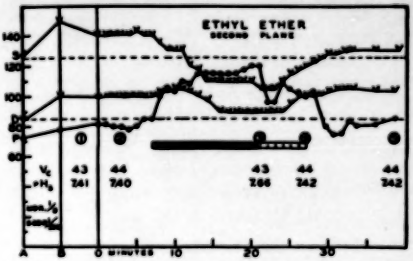


Chart 2.—Hyperventilation with oxygen during ether anesthesia. Legend as in chart 1.

when conducting artificial respiration is to hyperventilate the patient, particularly in emergencies.

The following experiments were therefore designed to study the functional effects of various grades of hyperventilation which might conceivably occur during anesthesia in man:

PROCEDURE

Patients of different age and sex with apparently normal cardiovascular and respiratory systems were selected who were to undergo short operative procedures. Data regarding pulse, arterial pressures and so on were obtained from the clinical record. When it was used, preliminary medication consisted of morphine sulfate and scopolamine hydrobromide in dosage appropriate to the age and condition of the patient. From one and one-half to two hours later, 0.5 to 1 cc. of capillary blood was obtained by finger incision, collected under oil and oxalated according to the procedure described by Shock and Hastings.[14] This and subsequent samples were analyzed in duplicate by the microtechnic of these authors and the following information obtained: hematocrit (V_c); hydrogen ion concentration of plasma (pH_a) [determined at 38 C.]; carbon dioxide content of whole blood ($CO_2)_b$. Determinations of carbon dioxide were made by the method of Van Slyke and Neill.[15] From these data the carbon dioxide tension (pCO_2) and the base bicarbonate ($BHCO_3)_a$ were calculated by the equation of Hasselbalch as modified by Hastings and Shock.

Several pulse (half minute observations) and arterial pressure determinations (auscultatory) were made at

11. Henderson, Yandell, and Haggard, H. W.: Respiratory Regulation of the CO_2 Capacity of the Blood: II. Low Levels of CO₂ and Alkali Induced by Ether; Their Prevention and Reversal: III. The Effects of Excessive Pulmonary Ventilation, J. Biol. Chem. **33**: 345 and 355 (Feb.) 1918.

12. Henderson, Yandell: Acapnia as a Factor in Postoperative Shock, Atelectasis and Pneumonia, J. A. M. A. **95**: 572 (Aug. 23) 1930.

13. Collip, J. B., and Backus, P. L.: The Effect of Prolonged Hyperpnea on the Carbon Dioxide Combining Power of Plasma, the Carbon Dioxide Tension of Alveolar Air and the Excretion of Acid and Basic Phosphate and Ammonia by the Kidney, Am. J. Physiol. **51**: 568, 1920. Kemp, W. N.: Tetany During Ether Anesthesia, Brit. J. Anesth. **11**: 169 (July) 1933.

14. Shock, N. W., and Hastings, A. B.: Studies of the Acid-Base Balance of the Blood: I. A Microtechnic for the Determination of the Acid-Base Balance of the Blood, J. Biol. Chem. **104**: 565 (March) 1934. Hastings, A. B., and Shock, N. W.: II. A Nomogram for Calculation of Acid-Base Data for Blood, ibid. **104**: 575 (March) 1934. Shock, N. W., and Hastings, A. B.: III. Variation in the Acid-Base Balance of the Blood in Normal Individuals, ibid. **104**: 585 (March) 1934.

15. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**: 523 (Sept.) 1924.

one minute intervals before anesthesia. A similar procedure was followed before, during and after hyperventilation. Anesthesia was induced in the supine position with ethyl ether, cyclopropane, tribromethanol 0.1 Gm. per kilogram, sodium amytal 0.01 Gm. per kilogram or morphine 0.08 Gm. and scopolamine 0.002 Gm. in divided doses. An orotracheal airway with cuff was inserted and the latter inflated. It was necessary to cocainize the pharynx and larynx when amytal, tribromethanol or morphine-scopolamine alone were used, in order that the orotracheal tube could be tolerated. The to and fro carbon dioxide absorption technic was employed with the canister placed close to the orotracheal tube to eliminate dead space. In addition to the agent, oxygen and small amounts of nitrogen completed the respired atmosphere except in one experiment in which air alone was used. When anesthesia had been established in a given plane, a second sample of capillary blood was obtained.

Hyperventilation was induced by two operators who alternately produced pressure on the breathing bag and pressure on the chest. The movements of both operators were rhythmic and all pressure changes were developed gradually rather than abruptly. The ventilation rates varied from 16 to 35 per minute. The intrapulmonic pressure developed at inspiration was not accurately determined but the maximum bag pressure varied from 20 to 30 mm. of mercury. An attempt was made to maintain a reasonably constant level of anesthesia (first or second plane) during hyperventilation with ether and cyclopropane, as judged by extrarespiratory signs. This objective was obtained in most instances, but if it varied the depth of anesthesia was decreased rather than increased. The arterial blood content of cyclopropane in one experiment, for example, was 6.9 volumes per cent at the beginning and 4.3 volumes per cent after fifteen minutes of hyperventilation.

The patients were observed closely during the periods of hyperventilation for signs of tetany. A sample of capillary blood was taken just before hyperventilation

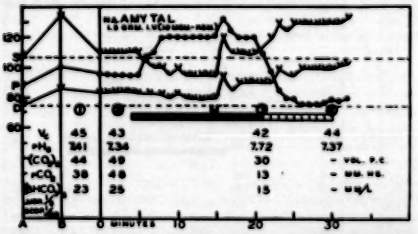


Chart 3.—Hyperventilation with oxygen during sodium amytal anesthesia. Legend as in chart 1. *M*, muscular activity (see text).

was discontinued. The last few inflations were made with pure oxygen and the bag left half filled with this gas (the pressure did not exceed atmospheric). The chest was exposed and the bag, chest and abdomen were observed closely for the return of activity. With the first spontaneous respiratory movement, the duration of apnea was noted and a blood sample obtained. Observations at one minute intervals were continued for at least twenty minutes after hyperventilation was discontinued and at five minute intervals throughout the subsequent operative procedure. In two cases hyperventilation was performed after the operative procedure had been completed in order to insure a more complete saturation and better equilibrium with the gaseous agents.

RESULTS

Hyperventilation of from eleven to twenty-one minutes' duration was produced in eleven patients. The degree of ventilation in some instances was as intense as could be obtained safely by manual methods. With the technical procedure employed it was impossible to

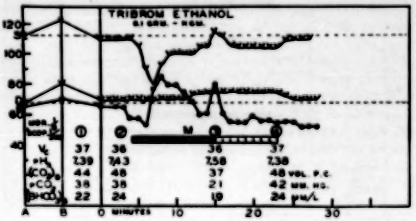


Chart 4.—Hyperventilation with oxygen during tribromethanol anesthesia. Legend as in chart 3.

determine the actual minute volume ventilation. The effectiveness of ventilation was determined entirely by the results of blood analysis. In two experiments, for example, the tension of carbon dioxide in arterial plasma was reduced to 9 and 10 mm. and the pH, increased to 7.73 and 7.71, respectively. A summary of the results obtained and a characterization of the acid-base displacements are presented in the accompanying tables.

Arterial Pressure.—Systolic: The character of the changes in systolic pressure during anesthesia with different agents will be noted in the charts. The fall is not precipitate as in the experiments on animals, probably because of differences in the intensity of hyperventilation. The slow decrease argues against a mechanical interference with the pulmonary or coronary circulation as a major factor in the arterial hypotension. A casual glance at the curves of systolic pressure in the accompanying charts is apt to be misleading since the final systolic levels during hyperventilation are more readily compared with the elevated levels which obtained during anesthesia. If such a comparison is made, a significant decrease in pressure will be noted in nearly every case, ranging from 2 to 60 mm. and averaging 25 mm. A comparison of the final systolic pressures during hyperventilation with the normal resting values taken before premedication or anesthesia (projected in the figures as the dotted lines) indicates, however, that the change in pressure is much less significant than the former method of comparison would indicate. On the latter basis of comparison, the mean fall with hyperventilation was only 10 mm., the range varying from a rise of 8 mm. to a fall of 25 mm. In no instance did the systolic pressure fall below an absolute value of 92 mm. The skin remained pink, dry and warm and there was no evidence of shock in any subject.

During apnea following hyperventilation, the systolic pressure increased rapidly during the first two minutes and more slowly thereafter until the original or a higher level was attained within a few minutes.

Diastolic: The diastolic pressure, as the systolic, is usually elevated during anesthesia, probably from the accompanying respiratory acidosis. When the final

diastolic pressures during hyperventilation are compared with the anesthesia levels it would appear as if respiratory alkalosis is usually associated with a fall in diastolic pressure, since this did occur in eight of the eleven cases. A slight rise occurred in the other three, but the mean for the group was a decrease of 10 mm. As with the systolic, comparisons based on the changes from the normal resting levels of diastolic

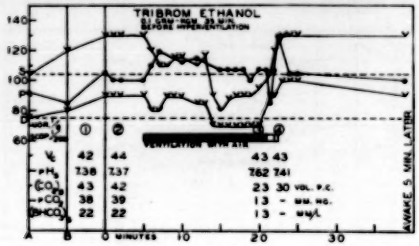


Chart 5.—Hyperventilation with air during tribromethanol anesthesia. Legend as in chart 1.

pressure lead to a different interpretation. Thus, the final diastolic levels, although reduced below the anesthesia levels in eight cases, still remain above the normal resting level in the majority of subjects. The change with hyperventilation varied from a decrease of 6 mm. to an increase of 16 mm., the average being an increase of 7 mm. These results indicate that narcosis of the grade induced in these experiments does not completely prevent the increase in the peripheral resistance which is known to occur in the normal subject during forced breathing.

When hyperventilation is discontinued, the recovery of diastolic and systolic pressures progresses rapidly and in a parallel manner. In some experiments the diastolic pressure increased to a level above the original and remained higher for several minutes after hyperventilation, although the systolic pressure was not elevated above the original level during the same period.

Pulse Pressure: The pulse pressure was uniformly reduced in these experiments but not below an absolute value of 20 mm., except during amytal anesthesia (chart 3). A reduction in pulse pressure is usually interpreted to indicate a diminished stroke volume. Norlin [4] has shown that forced ventilation in the normal individual is associated with an increased cardiac output which is proportional, within reasonable limits, to the degree of overbreathing. Roome [16] observed values for cardiac output of from 84 to 110 per cent of normal in the hyperventilated dog during anesthesia. Experimentally,[17] it is known that alkalosis increases the tone and irritability of cardiac muscle. It is interesting to note that the larger reduction in pulse pressure occurred during anesthesia with ether (chart 2), amytal (chart 3) and morphine-scopolamine (chart 6). These agents are known to depress the peripheral vagus. The heart rate increase was also larger in these experiments. It is not improbable that the vagal influence modifies the direct effects of alkalosis on the heart and that its removal constitutes a disadvantage.

16. Roome, N. W.: Cardiac Output in Hyperventilation, Proc. Soc. Exper. Biol. & Med. **28**: 939 (June) 1931.

17. Jerusalem, E., and Starling, E. H.: Significance of Carbon Dioxide for the Heart Beat, J. Physiol. **40**: 279, 1910. Schlapp, W.: Adrenalin and Ventricular Fibrillation in the Decapitated Cat, Quart. J. Exper. Physiol. **23**: 335 (Aug.) 1933.

Heart Rate.—Norlin [4] observed a uniform increase in pulse rate during forced breathing in the normal subject. No significant change in heart rate was associated with hyperventilation during cyclopropane anesthesia (chart 1), the average value during anesthesia in five cases being 65 and during hyperventilation 70. These slow rates are of vagal origin. A rise of from 20 to 40 beats per minute occurred during ether, tribromethanol and amytal anesthesia. Hyperventilation increased slightly the rapid rate which obtained during morphine-scopolamine narcosis. No arrhythmias were detected by palpation of peripheral arteries during hyperventilation.

The heart rate was usually reduced further or increased slightly in apnea during cyclopropane anesthesia. With the other agents, the rate decreased from the higher level attained during hyperventilation.

Respiration.—The duration of apnea following hyperventilation varied from five to nine minutes in nine subjects who were hyperventilated with oxygen during complete anesthesia. No cyanosis or other alarming signs were observed in any of these subjects before respiration was resumed. It is to be remembered that in these experiments the narcosis was not deeper than second or third plane surgical anesthesia. The long period of apnea is probably related in part to the effects of the anesthetic but in large measure to the fact that the stimulus of anoxia was lacking. Norlin [4] found that the period of apnea in normal subjects, even after vigorous hyperpnea with air for one hour, was only fifteen to twenty seconds. The results presented here cannot be compared directly with his, however, since the duration of ventilation is different. It has been observed in the dog that the period of apnea becomes shorter as the duration of ventilation is prolonged. Apnea is greatly prolonged in the normal subject if hyperventilation is accomplished with oxygen.[18]

The influence of oxygen can be observed readily in two experiments with tribromethanol anesthesia, in

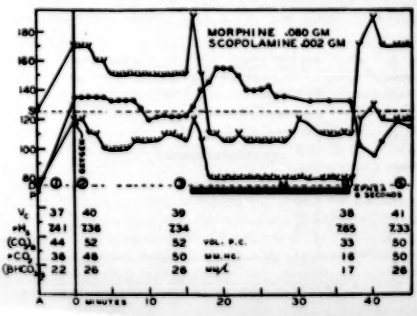


Chart 6.—Hyperventilation with oxygen during morphine-scopolamine narcosis. Legend as for chart 3.

which patient 9 (chart 4) was hyperventilated with oxygen and patient 10 (chart 5) with air. Although apnea lasted eight minutes without cyanosis in patient 9, moderate cyanosis was observed during the ninety second apnea in patient 10. It is interesting to compare the levels of pH, and the carbon dioxide at which

18. Vernon, H. M.: The Production of Prolonged Apnoea in Man, J. Physiol. **38**: 18, 1909. Hill, L., and Flack, M.: The Influence of Oxygen Inhalations on Muscular Work, ibid. **40**: 347, 1910. Boothby, W. M.: Absence of Apnoea After Forced Breathing, ibid. **45**: 328, 1912.

V 19

breathing was resumed in these two cases. In patient 9 both the pH_a and the carbon dioxide content had returned to the levels which obtained before hyperventilation. In patient 10, breathing began while the carbon dioxide content was still 12 volumes per cent below the level present before hyperventilation. It was not possible to calculate accurately the carbon dioxide tension or the base bicarbonate in this experiment because of the oxygen unsaturation of hemoglobin.

In one experiment during morphine-scopolamine narcosis, the period of apnea was only eight seconds although the subject had been hyperventilated with oxygen for twenty-one minutes. This remarkable difference is difficult to explain except on the basis of a scopolamine effect. It cannot be denied that scopolamine exerts an antidotal action on the respiratory effects of morphine in man.[19] It is difficult to believe that such a short period of respiratory arrest would have occurred after 80 mg. of morphine without scopolamine, although the final answer will await experiment. It must be presumed on theoretic grounds that the oxygen delivery to the tissues is reduced in these experiments because of the known shift in the oxygen dissociation curve with alkalosis. It is improbable, however, that tissue anoxia served as the stimulus to breathing in the case with morphine-scopolamine any more than in the experiments involving other agents. Since anoxemia was absent, it is difficult to invoke carotid body stimulation to account for the short apnea in this subject. It is of interest to compare the levels of carbon dioxide and pH_a at which the first breath occurred with the level immediately preceding hyperventilation (table 2). The close similarity in values is striking except in patients 10 and 11. These results indicate further that an anoxemic stimulus to respiration was absent in most of the experiments.

At the termination of hyperventilation, the chest was allowed to assume its own position. Whereas this position is the expiratory one and the accessory muscles are relaxed, it is not the type of chest observed with complete intercostal nerve paralysis due to the action of a narcotic drug. The intercostal muscles still retained their tone, and at the first inspiratory effort these muscles, as well as those of the diaphragm, were involved in the respiratory act.

Tetany.—The duration of hyperventilation was similar, and the degree of acid-base displacement was of the same order, or even slightly greater, than that obtained by Shock and Hastings[20] during voluntary hyperpnea in man. All of their six subjects but one exhibited tetany. Numerous observers have reported tetany following hyperpnea, whether induced voluntarily[21] or as a result of anxiety states or disease.[22] Tetany or muscle movement did not accompany hyperventilation during cyclopropane or ether anesthesia. Evidently the depressant effects of these narcotics are sufficient to prevent entirely the increased muscular activity.

Although the characteristic tetany was not observed, flexion of the thighs on the trunk occurred, a Babinski reflex was present, and tendon reflexes were exaggerated during hyperventilation with tribromethanol anesthesia. During amytal anesthesia, hyperventilation induced flexion of the legs and fingers although the patient was in third plane anesthesia as judged by respiratory signs, preceding and following hyperventilation. During morphine-scopolamine narcosis, movements of large muscle groups and rigidity of the limbs were noted. The patellar and triceps reflexes were exaggerated and a Babinski reflex was present. When muscular activity was present during hyperventilation, it was invariably associated with a rise in both systolic and diastolic arterial pressures. This rise was sustained for several minutes. One subject vomited during very light cyclopropane anesthesia after eight minutes of ventilation. The arterial pressure immediately rose to levels considerably above the original.

All of the agents used in these experiments, with the exception of morphine-scopolamine, prevent the tetany of alkalosis. This observation casts doubt on the concept that respiratory alkalosis is an etiologic factor of significance in "ether spasm" or general convulsions during deep anesthesia with ether or other agents.

Hematocrit.—Since hyperventilation was done with an atmosphere saturated with water vapor, the fluid loss during hyperventilation was probably small, and the hematocrit values should be of interest. Almost without exception there was a slight decrease in cell volume. Whereas this change is not large and may not be significant, the trend is indicated. These results differ from those of Shock and Hastings, who noted an increase in cell volume in the unanesthetized subject. Since their subjects were presumably losing water through the lungs, the blood concentration may possibly be accounted for on this basis. It is possible that oxygen played a role, since a slight rise occurred in patient 10, who was hyperventilated with air only.

Base Bicarbonate (alkali reserve).— The base bicarbonate was reduced significantly during hyperventilation. This is due in part to an appreciable increase in acid metabolites such as lactic acid[23] and the ketone bodies.[24] At the end of the period of apnea in these experiments (except the morphine-scopolamine case) the base bicarbonate had returned to the prehyperventilation values. If hyperventilation had been continued longer, a certain portion of the base would undoubtedly have been eliminated in the urine or lost to the tissues, and the recovery of the original level would probably have been slower. During ether anesthesia the elevation in plasma pH was not as great as that obtained in other experiments although the hyperventilation was equally severe. This may be due to a greater production of acid metabolites. In this experiment, values for base bicarbonate were not obtained since ether interferes with the analysis for carbon dioxide.

General Effects.—No untoward effects were observed as a result of these procedures. Some of the subjects hyperventilated during cyclopropane anesthesia were awake within five to ten minutes after resumption of spontaneous breathing. Films of the chest taken before and after hyperventilation during ether anesthesia were identical in clarity although the usual postoperative elevation of the diaphragm was noted. The post-

19. Waters, R. M.; Bennett, J. H., and Leigh, M. D.: Effects on Human Subjects of Morphine and Scopolamine Alone and Combined, J. Pharmacol. & Exper. Therap. **63**: 38 (May) 1938.

20. Shock, N. W., and Hastings, A. B.: IV. Characterization and Interpretation of Displacement of the Acid-Base Balance, J. Biol. Chem. **112**: 239 (Dec.) 1935.

21. Grant, S. B., and Goldman, A.: A Study of Forced Respiration: Experimental Production of Tetany, Am. J. Physiol. **52**: 209 (June) 1920. Schneider:[a] Henderson, Prince and Haggard.[b]

22. Bielschowsky, P., and Mandowsky, C.: Ueber Zustand und Zustandsänderung in Säure-Basengleichgewicht bei der Pathogenese der Hyperventilationstetanie, Ztschr. f. klin. Med. **114**: 470, 1930. Harwood,[c] Kerr, Dalton and Gliebe.[d]

23. Kodera, K., and Sugimoto, H.: Der Kohlehydrat- und Gasstoffwechsel im Muskel bei Hyperventilationsalkalosis, Tohoku J. Exper. Med. **24**: 37 (Sept. 28) 1934.

24. Frank, E.; Leiser, R., and Weisz, S.: Ueberventilations-acetonurie und Ueberventilations-lactacidurie (-lactacidaemie): Scheinacidosen und ihre klinische Bedeutung, Ztschr. f. klin. Med. **114**: 219, 1930. Paschkis, K., and Buttu, G.: Untersuchungen ueber die Hyperketonamie bei Hyperventilation und anderen alkalotischen Zuständen, ibid. **123**: 764, 1933.

operative course was uneventful in all patients. Electrocardiographic records were taken at one minute intervals during hyperventilation and continuously during the period of apnea in patient 10. When hyperventilation was discontinued, the pulse rate was reduced within thirty seconds from 115 beats to 85 beats a minute. Two ventricular extrasystoles were noted at this time. These were the only arrhythmias which were observed and were probably of vagal origin. During hyperventilation the T wave disappeared. Barker, Shrader and Ronzoni [23] have described recently a flattening of the T wave during alkalosis from hyperventilation or alkali administration.

COMMENT

The results presented here do not lend support to a hypothesis of shock based on acapnia as originally defined. The term acapnia has been studiously avoided in the present discussion. While the word as originally used had a precise though limited meaning, it has come to be a term without definition, convenient in its vagueness for the designation of any state of decreased vitality. Henderson [12] says:

> The most practical definition of acapnia is that of an acute condition involving disturbances and depression of various functions, all of which are relieved and restored to normal by the inhalation of carbon dioxide.

This is an unfortunate state of affairs, since by such a definition it is difficult to establish an adequate rationale for the therapeutic use of carbon dioxide. Although carbon dioxide in certain concentrations serves as a pharmacologic agent and stimulates specific groups of nerve cells, the deduction that the initial cause of the nerve cell depression is a "carbon dioxide deficit" is difficult to justify. It would be as logical to state that epilepsy is due to a deficit of phenobarbital, since the latter compound is effective in the treatment of this condition.

Narcotic drugs depress certain physiologic mechanisms which allow the non-narcotized individual to compensate, in part at least, for a rapidly induced respiratory alkalosis. The circulatory changes and general signs which occurred in these experiments were in no respect comparable to those of traumatic or surgical shock, although the rapidity and extent of carbon dioxide loss greatly exceeds that which is likely to occur in clinical practice. It appears to be reasonable to take the position that the adverse effects of respiratory alkalosis on the circulation or on the general vitality, even during anesthesia, have been overemphasized. When these observations are correlated with those from the literature, the apparent differences between the response to respiratory alkalosis of the dog and man no longer exist, since without narcosis, and in these experiments even during narcosis, a significant arterial hypotension does not occur. The experiments presented here were of relatively short duration. The results obtained are so similar to those obtained in the dog that it seems safe to infer that a gradual recovery of arterial pressure would have occurred with longer hyperventilation, and that a similar and immediate return to normal would have been observed when hyperventilation was discontinued.

SUMMARY

Eleven subjects were manually hyperventilated for periods of eleven to twenty-one minutes during anesthesia with different agents.

A marked respiratory alkalosis was developed, the average increase in plasma pH being 0.31 unit from anesthesia level and 0.25 unit above normal level.

The carbon dioxide tension in arterial blood was reduced, on the average, 21 mm. below the mean level during anesthesia and 31 mm. below the mean normal level before anesthesia.

Systolic and diastolic arterial pressures were reduced during hyperventilation from the elevated levels of anesthesia, the average decrease being 25 mm. systolic and 10 mm. diastolic. The decrease from the normal systolic levels before anesthesia, however, averaged only 10 mm., whereas the mean change in diastolic pressure was an increase of 7 mm. above the normal before anesthesia.

The initial arterial pressures were reestablished rapidly when hyperventilation was discontinued, and no adverse effects on the circulation or general condition of the patient followed hyperventilation.

The duration of apnea varied from five to nine minutes without accompanying cyanosis when hyperventilation was performed with oxygen. In one subject hyperventilated with air, apnea lasted one and one-half minutes and was accompanied by moderate cyanosis.

Cyclopropane and ether prevented entirely the tetany of alkalosis, whereas amytal, tribromethanol and morphine-scopolamine did not entirely prevent, but modified, the character of the muscular phenomena.

CONCLUSIONS

These data, when compared with the effects of voluntary hyperpnea in man and correlated with the results of carefully controlled mechanical hyperventilation of anesthetized and unanesthetized dogs, prove that the arterial hypotension due to the rapid removal of carbon dioxide is a phenomenon which obtains only during anesthesia. Furthermore, it is incorrect to classify this hypotension as surgical shock, since (*a*) the hypotension is not progressive, (*b*) recovery of arterial pressure occurs even during continued ventilation and, (*c*) when hyperventilation is discontinued, recovery is immediate.

ABSTRACT OF DISCUSSION

DR. HENRY K. BEECHER, Boston: This field, as the speaker has pointed out, is extremely confused. It is stated that "the two greatest errors in the use of carbon dioxide in anesthesia consist in attempts to superimpose a respiratory acidosis on an acidosis of metabolic origin, and its use in asphyxial states in which blood and tissue tension of carbon dioxide are already so high as to be at a depressant level." It must be granted that carbon dioxide unwisely used may produce toxic effects. The use of carbon dioxide by anesthetists occurs chiefly on two occasions: To promote induction and to speed up recovery. Occasionally patients are encountered who are slow to be anesthetized. The induction may be speeded up in two ways: By increasing the concentration of the anesthetic agent; this has obvious drawbacks. By increasing the respiratory minute volume by the use of carbon dioxide; this seems to be the more desirable alternative. The desirability of using carbon dioxide can be determined in a given case by a simple physiologic test: Suppose carbon dioxide is added to the inspired gases to the extent of 5 per cent for one minute. If the patient is in the critical condition described, the addition of the carbon dioxide should further depress him and it can then be stopped, without serious effect. If, on the contrary, the respiration is stimulated, the use of a low percentage of carbon dioxide is permissible for the few minutes required to complete the induction, for if a seriously high blood carbon dioxide level had existed, the respiratory stimulation would not have occurred. Hyperventilation leads to considerable circulatory disturbance. The safety of hyperventilation is questioned by their finding that one dog in eighty did have a fatal circulatory failure. Apparently this

23. Barker, P. S.; Shrader, E. L., and Ronzoni, Ethel: Effects of Alkalosis and Acidosis on the Human Electrocardiogram, Am. Heart J. **17**: 169 (Feb.) 1939.

dog had a diseased heart. When one considers the ease with which cardiac disease can be overlooked in man, doesn't this at least offer a warning? "Controlled respiration," that is, the production of apnea and the placing of the respiration at the discretion of the anesthetist, removes one of the most valuable safeguards of the circulation. The gradual onset of respiratory failure and ultimate respiratory paralysis are of importance as warnings that the blood concentration of the anesthetic agent is getting too high for circulatory safety. These warnings are of importance for the expert and are indispensable for the less than expert. Ten cases seems too few to allow any certainty of conclusion as to the effects of hyperventilation under a specific anesthetic agent. This remark is emphasized when it is recalled that several anesthetic agents are concerned in the ten cases. This paper shows that in ten cases shock did not occur as a result of hyperventilation during anesthesia. It is a step toward the elimination of misconception as to the limits of usefulness of carbon dioxide.

DR. M. H. SEEVERS, Madison, Wis.: We are not advocating hyperventilation as a procedure in anesthesia; we have merely made an experimental attempt to establish whether or not hyperventilation, even to the maximum which can be obtained by ordinary clinical procedures, produces a shocklike state. If we may be allowed to draw an analogy with the effects on the dog, I might say that such a shocklike state does not occur in a dog even though hyperventilation is conducted for eight or ten hours. The animals recover after this period even though the pressure of carbon dioxide in arterial blood is maintained at as low as 8 mm. I think the deleterious effects of carbon dioxide loss on the cardiovascular system have been greatly overemphasized.

AVITAMINOSIS OCCURRING IN DIABETIC PATIENTS UNDER INSULIN THERAPY

V. P. SYDENSTRICKER, M.D.
L. E. GEESLIN, M.D.
AND
J. W. WEAVER, M.D.
AUGUSTA, GA.

The frequent occurrence of glossitis and stomatitis in persons with diabetes is a matter of common knowledge. The usual explanation of such lesions, particularly when complicated by monilial or spirochetal infection, has been "lowered resistance" or "a toxic state" due to hyperglycemia. Since the type of glossitis and stomatitis usually seen in diabetes is in all respects similar to that seen in mild endemic pellagra or in acute pellagra secondary to parenteral nourishment with dextrose solutions, it seems probable that the cause may be an avitaminosis caused by abnormal carbohydrate metabolism. Three cases recently observed would seem to substantiate this hypothesis. In two instances, signs of avitaminosis developed when carbohydrate intake and insulin dosage were rapidly increased; in the third, signs of nicotinic acid and riboflavin deficiency were present on admission, disappeared for a short time under an abundant diet and small doses of insulin but recurred when the diet and the insulin were increased.

REPORT OF CASES

CASE 1.—L. S., a white woman aged 58, admitted to the hospital Jan. 10, 1939, was known to have diabetes and had been observed in an outdoor clinic and was well maintained over a long period on a diet containing 70 Gm. of protein, 70 Gm. of fat and 150 Gm. of carbohydrate with 45 units of protamine zinc insulin daily. Her present complaint was an abscess of the left side of the neck of one week's duration. She was admitted to the surgical service, where it was found that she was well nourished and developed with an obvious deep infection of the left side of the neck. General physical examination was not important. The blood showed 9.2 Gm. of hemoglobin per hundred cubic centimeters and 4,100,000 erythrocytes and 8,400 leukocytes per cubic millimeter. The blood sugar was 200 mg. per hundred cubic centimeters. The urine showed large amounts of sugar and "2 plus" acetone. The diet and insulin that had sufficed for control were continued. The abscess was incised and drained on the day following admission and an attempt was made to control glycosuria and ketosis with added dextrose and insulin. Because the patient became disoriented and glossitis developed she was transferred to the medical service January 30. On transfer she was disoriented and actively delirious; the tongue was bright red and atrophic and it was thought that she had pellagra. Nicotinic acid was given intravenously, 200 mg. a day for seven days. During this time she became quite rational and the glossitis healed. Because of persistent hyperglycemia and glycosuria protamine zinc insulin was increased on February 6 to 50 units, on the 13th to 60 units and on the 18th to 65 units. On the 20th severe glossitis recurred, and on the following day ulceration was added to the fiery redness of the tongue. Nicotinic acid was given, 100 mg. daily by mouth from February 20; there was rapid resolution of glossitis and stomatitis and improvement in appetite. On the 26th it was noted that the tongue looked normal. On this day the diet was reduced to protein 40 Gm., fat 40 Gm. and carbohydrate 120 Gm., and protamine zinc insulin was reduced to 50 units. Nicotinic acid was discontinued. Improvement continued and on March 6 protamine zinc insulin was reduced to 40 units with good control of the diabetic symptoms. The patient has continued to be well controlled from the standpoint of her diabetes, and glossitis has not recurred.

CASE 2.—M. H., a white woman aged 67, admitted Jan. 30, 1939, complained of pain in the right hip joint. She was known to have had diabetes for ten years and had been well maintained on a diet containing protein 40 Gm., fat 70 Gm. and carbohydrate 100 Gm., with protamine zinc insulin 25 units daily. Three years ago she suffered a fracture of the right femur and had been ambulant on crutches since; a week before admission she fell again and thereafter was unable to use the right leg. Examination showed that she was well developed and slightly obese, with a second fracture of the right femur. She was slightly disoriented and there was some redness of the tongue. The blood showed 10.2 Gm. of hemoglobin per hundred cubic centimeters and 4,350,000 erythrocytes and 9,500 leukocytes per cubic millimeter. The blood sugar was 280 mg. per hundred cubic centimeters. The urine showed large amounts of sugar and acetone. She was given appropriate orthopedic treatment and continued on the same diet and dosage of insulin that had sufficed at home, but delirium continued and there was persistent hyperglycemia with glycosuria and ketosuria. February 7 she was transferred to the medical service, where it was found that the tongue was bright red and fissured and that diabetes was not controlled. Diet was continued as before and protamine zinc insulin was increased to 45 units a day. Nicotinic acid was given intravenously, 100 mg. a day on February 7, 8 and 9, with marked improvement in the mental state and of glossitis. Glycosuria and hyperglycemia persisted, and the dose of protamine zinc insulin was increased on February 13 to 50 units, on the 15th to 55 units and on the 18th to 65 units. On the 18th the tongue became fiery red and the patient was again disorientated, glossitis grew rapidly worse and delirium developed, requiring restraint. On the 20th nicotinic acid was given by mouth, 100 mg. daily. By February 24 there was some improvement in glossitis, and delirium had cleared so that the patient could go without restraint and sat up. Because glossitis persisted nicotinic acid was increased to 200 mg. a day on March 3, 300 mg. on the 5th and 400 mg. on the 7th. Following the last increment of nicotinic acid there was rapid paling of the tongue and some regeneration of papillae. Diabetes was entirely controlled by diet and the amount of insulin given and the patient was dismissed March 13.

CASE 3.—K. W., a white woman aged 58, admitted March 1, 1939, complained of an ulcer on the right great toe. Before admission it had been found that she had severe glycosuria and

From the Department of Internal Medicine, University of Georgia School of Medicine and the University Hospital.

ketosuria. She was slightly obese and well developed. There was edema of the ankles and feet. The mouth showed deep fissures at the commissures of the lips with slight reddening and desquamation of the mucocutaneous junctures. The tongue was red and atrophic. The heart was moderately enlarged with a soft systolic murmur at the mitral area and a much accentuated aortic second sound. The blood pressure was 176 systolic, 110 diastolic. There was moderate vaginitis with a seropurulent discharge. The blood contained 13.5 Gm. of hemoglobin per hundred cubic centimeters and 4,600,000 erythrocytes and 9,000 leukocytes per cubic millimeter. Blood sugar was 330 mg. per hundred cubic centimeters. The urine showed large amounts of sugar and a trace of acetone. The diet prescribed contained 50 Gm. of protein, 50 Gm. of fat and 150 Gm. of carbohydrate; 15 units of protamine zinc insulin was to be given each morning. Insulin was increased March 4 to 25 units and on the 6th to 40 units to control glycosuria and hyperglycemia. The tongue and labial lesions healed rapidly during the first three days of treatment so that on March 6 the fissures at the corners of the mouth were healed and the tongue was of normal color. March 9 there was sudden recurrence of the commissural fissures, which were extremely painful, and the tongue was again red and tender. March 11, 10 mg. of riboflavin was given intramuscularly and, because no improvement was noted by March 13, 25 mg. was given by the same route. By March 15 the fissures at the corners of the mouth were healed but the tongue remained very red and somewhat tender. Protamine zinc insulin was increased on March 17 to 50 units and the diet was augmented by 10 Gm. of protein and 20 Gm. of carbohydrate. On March 19 the rhagades reappeared and the tongue was more red and painful. Riboflavin was given by mouth, 20 mg. a day from March 19 to March 25. There was improvement in the cheilitis on March 24 and by the 27th the right corner of the mouth was entirely healed; the left remained slightly red. Nicotinic acid was begun on March 26, 100 mg. a day by mouth. The tongue was pink and of good texture by March 29 and the fissures at the left oral commissure persisted. It seems likely that the marginal stomatitis will recur.

COMMENT

Two patients with complications of diabetes developed clinical signs of pellagra when the carbohydrate content of the diet was increased, and added insulin was administered to assure utilization of the augmented diet. In both cases nicotinic acid controlled the glossitis and mental symptoms but when carbohydrate or insulin was again increased the symptoms recurred and were again relieved by nicotinic acid. One patient who probably had an inadequate diet at home showed evidence of both nicotinic acid and riboflavin deficiency on admission. On a therapeutic diet with small amounts of insulin, signs of avitaminosis disappeared but recurred promptly with increase in the dose of insulin. Riboflavin given intramuscularly seemed to cure cheilitis but there was a prompt relapse after insulin was increased. Riboflavin and nicotinic acid seemed to cause much improvement in the signs and symptoms of avitaminosis. It would seem likely that rapid metabolism of carbohydrate such as is secured in diabetic patients by the use of insulin causes correspondingly rapid depletion of coenzymes and may in this way produce signs and symptoms of avitaminosis. There is at present no adequate explanation of the occurrence of avitaminosis under such conditions except that suggested. Since the diets given these patients were adequate in all vitamins, the question of inadequate absorption or storage must be given consideration. More important would seem the fact that coenzymes I and II both contain nicotinic acid, and it is quite possible that the great increase in dextrose metabolism caused by relatively large amounts of insulin might exhaust the body stores of this vitamin. The results of vitamin therapy in the cases under consideration would seem to confirm this hypothesis.

Since this report has been in preparation, observations have been published indicating that coenzymes are much depleted in diabetic patients with severe ketosis.[1] The experience of these authors in this work would seem to corroborate the conclusions that we have reached. Severe ketosis may follow exhaustion of coenzymes and logically might be expected to do so. Under chronic conditions, signs of avitaminosis might be expected to appear, with or without ketosis, when unusually rapid dextrose metabolism is brought about by the use of insulin.

HYPOSPADIAS

OBSERVATIONS ON ITS SURGICAL CORRECTION

CHARLES MORGAN McKENNA, M.D.

CHICAGO

The best evidence that no standard operation for the correction of the hypospadic deformity has been recognized by the surgical profession is the variety of methods employed by different men to achieve the same end result. It is obviously impossible in a short article such as this one to name all the authors who have contributed to this field, but one should mention Duplay,[1] Ombrédanne,[2] Thiersch,[3] Nové-Josserand,[4] Bucknall[5] and Beck[6] among the older writers and Blair,[7] Cabot,[8] Cecil,[9] Crabtree,[10] Hagner,[11] O'Conor,[12] Lowsley,[13] Higgins, Clinton Smith[14] and Young[15] among the later writers.

IMPORTANCE OF CORRECTING THE PENILE CURVATURE

There are two prominent features of every hypospadic deformity: the defective urethra and the ventral curvature of the penis. There may be other associated pathologic changes such as undescended testicles, but the two conditions mentioned are found to some degree in every case.

My purpose in this paper is not so much to deal with the construction of a new urethra as to emphasize the necessity for correction of the curvature of the penis before attempting to form the new urethra. The amount of curvature of the penis varies in different

1. Vilter, R. W.; Vilter, S. P., and Spies, T. D.: Am. J. M. Sc. **197**: 322 (March) 1939.

From the College of Medicine and the Research and Educational Hospitals of the University of Illinois.

Read before the Section on Urology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.

The testosterone propionate (perandren), which was valuable in the author's results, was supplied by the Ciba Pharmaceutical Products, Inc., Summit, N. J., through Dr. E. Oppenheimer.

1. Duplay, Simon: Arch. gén. d. méd. **133**: 513, 1874; **145**: 257, 1880; Bull. et mém. Soc. de chirurgiens de Paris **6**: 169, 1880.

2. Ombrédanne, Louis: Bull. et mém. Soc. de chir. de Paris **37**: 1076, 1911; **38**: 449, 1912; Monde méd. **36**: 521, 1926.

3. Thiersch, Karl: Arch. d. Heilk. **10**: 20, 1869.

4. Nové-Josserand, Gabriel: Lyon méd. **85**: 198, 1897; **100**: 278, 1907; **108**: 923, 1907; Bull. Soc. de chir. de Lyon **7**: 325, 1904; **8**: 343, 1905; **10**: 184, 1907; Arch. gén. de chir. **4**: 331, 1909; J. d'urol. **5**: 393, 1914; **8**: 30, 1920.

5. Bucknall, R. T.: Lancet **2**: 887, 1907.

6. Beck, C.: New York M. J. **67**: 147, 1898; **70**: 212, 1899; **72**: 969, 1900; **90**: 289, 1909.

7. Blair, V. P.; Brown, J. B., and Hamm, W. J.: Surg., Gynec. & Obst. **57**: 646 (Nov.) 1933. Blair, V. P., and Byars, L. T.: J. Urol. **40**: 814 (Dec.) 1938.

8. Cabot, Hugh; Walters, Waltman, and Counseller, V. S.: Read at the meeting of the American Urological Association, Atlantic City, N. J., 1934.

9. Cecil, A. B., in Cabot, Hugh: Modern Urology, ed. 3, Philadelphia, Lea & Febiger, 1936.

10. Crabtree, E. G., quoted by Cecil.[9]

11. Hagner, F. R., and others: Tr. Am. A. Genito-Urin. Surgeons **15**: 11, 1922.

12. O'Conor, V. J.: Oral communication to the author.

13. Lowsley, O. S., and Begg, C. L.: A Three-Stage Operation for the Repair of Hypospadias, J. A. M. A. **110**: 487 (Feb. 12) 1938.

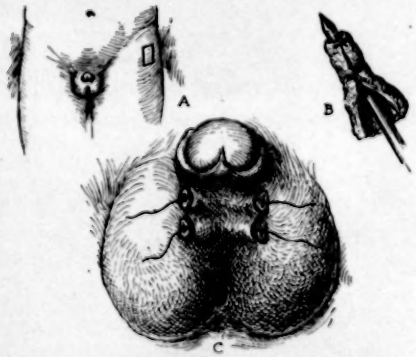
14. Smith, Clinton: J. Urol. **40**: 239 (July) 1938.

15. Young, H. H., and Davis, D. M.: Practice of Urology, Philadelphia, W. B. Saunders Company, 1926.

cases, usually being most marked when the urethral opening is farthest from the glans, that is, the perineal type. According to some authors this curvature is due to a thickening and contraction of Buck's fascia, while others contend that it is due to a lack of development of the corpus spongiosum, since there is no urethra present. Whatever the exact cause, a firm inelastic cord is present on the ventral surface of the penis which, as the corpora cavernosa develop, tends to pull the distal end of the penis downward and inward, curving it as a bow-string bends a bow. As the corpora cavernosa lengthen during erection, the curvature is of course much exaggerated, causing the penis to assume the shape of an inverted U.

Sometimes the shortening is not sufficiently marked to cause curving when the penis is flaccid but on erection a curve or crook appears. Sometimes the urethral opening may be quite close to its normal location and the possibility of this curving on erection is not thought of. It is a point that must be exactly determined before any plan of procedure is formulated.

When one reviews the literature, including the textbooks, it is interesting to note how little attention is given to correction of the deformity as compared to the enormous space given over to discussion of the



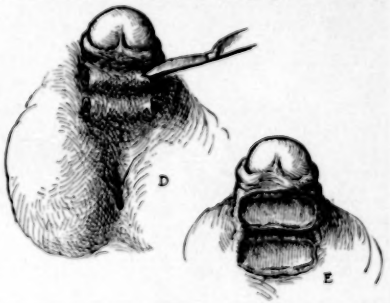


Fig. 1.—Technic of Hagner's tunnel graft method for correction of the ventral curvature. *A*, donor site for the graft; *B*, forming the graft into a tube about the trocar; *C*, tubular grafts in place; *D*, opening the tubular grafts at the second stage; *E*, tubular grafts opened out, adding to the length of the ventral surface of the penis.

methods of urethral reconstruction. The penis serves two purposes: it is primarily an organ of copulation and only secondarily, however conveniently, a drain for the bladder. Therefore in the surgical correction of hypospadic deformities both these functions must be kept in view, and in the order of their relative importance.

Too often the construction of the urethra is the only phase thought of, or else the correction of the curvature is considered a minor preliminary to the urethral plastic operation and is given scant care and attention. In our clinic at the Illinois Research and Educational Hospitals we have seen many patients who had had good anatomic reconstructions of the urethra elsewhere but in whom good functional results had not been achieved. This was due to the fact that, while the urethra came to the end of the penis, the urethra was so short that some still had to sit down to urinate, and even those who could urinate standing found normal erection impossible. Some patients said that the curvature was worse than before the operation had been done. The patients were little if any better off than they were before the surgical intervention. Uncritical examination of these cases would lead one to believe that they were good end results and probably were so considered by the surgeons responsible. The adult patients, however, felt otherwise.

OPTIMAL AGE FOR OPERATION

I believe that age is an important factor in the results in this work. In my experience, from 12 to 14 years seems to be the proper time to begin. However, I have seen children who at 11 years and occasionally earlier had genitalia and sex characteristics as well developed as those of a child of 14. Therefore the individual conditions present in any case govern the decision as to the optimal time for surgery. The younger the child, the more difficult the operation, because the parts are small and less easily managed. In cases in which the tunnel graft method is used to correct the curvature it may be performed when the boy is from 8 to 10 years old and the urethral reconstruction postponed a few years.

TESTOSTERONE AS A PREOPERATIVE MEASURE

In a number of cases we have used testosterone propionate (perandren) judiciously. When the genitalia are small and the urethral opening is far back in the perineum, the use of testosterone propionate may be indicated. It not only develops the genitalia but tends to bring the urethral opening forward, both of which results simplify the construction of the new urethra. Often a hypospadic child of 14 years will have genital organs of a size normal for a child of 7 or 8 years. The value of the intelligent use of this drug in these cases should be emphasized.

THE TUNNEL GRAFT METHOD OF HAGNER

Correction of the Deformity.—My first work on the correction of the downward curvature was patterned after the tunnel graft method of Francis Hagner. It was in most cases satisfactory but it necessitated at least two operations before the desired correction was obtained. As many as four tunnel grafts were sometimes necessary to accomplish the desired correction and obtain a penis that was straight when in erection. Some of the grafts were less satisfactory than others, owing to the amount of slough and the time before the denuded area was epithelized.

Dr. Vincent J. O'Conor and I, independently of each other, began using the tunnel graft at about the same time. We have operated on about the same number of patients with this method and a comparison of our results show that they are equally satisfactory.

The Hagner Technic.—This method utilizes free whole-thickness grafts of hair-free skin. As stated, this work may be done a little earlier than the urethral construction, depending on the size of the penis. An attempt is made before the time of operation to estimate the number of grafts that will be necessary. Each tunnel graft should add from 1 to 1.5 cm. to the length of the ventral surface of the penis.

An area on the thigh is selected which is as hair free as possible (fig. 1 *A*). A 16 F. trocar is used to introduce the grafts, and the size of the graft is determined by wrapping gutta-percha or metal foil around the trocar and cutting a pattern of the proper size. A

Fig. 2.—Transverse incision for dissection of the fibrous tissue.

piece of skin the size of the pattern is then dissected up from the donor site previously selected. In the original Hagner work some fat was lifted with the skin. We remove the skin with as little subcutaneous tissue as possible and it has proved more advantageous.

The skin graft is then wrapped around the trocar with the cutaneous surface inside and the edges sutured together with interrupted sutures of fine chromic catgut (fig. 1 *B*). In this way a tube of skin is formed. The trocar carrying the graft is then pushed transversely through the penis beneath the fibrous cord on the ventral surface. It is necessary to make a small incision on each side of the penis at the points of entrance and exit of the trocar. The tubular graft is so oriented that the suture line is nearest the ventral surface of the penis. The trocar is then removed and the ends of the tube are sutured to the edges of the cutaneous incisions on each side with a few interrupted silk sutures. A piece of silkworm gut is threaded through the tunnel and left in a large loop to keep the opening clear for drainage of any blood or serum that might otherwise collect (fig. 1 *C*). When more than two tunnel grafts are necessary it is probably best to introduce only two at one sitting and do the others later.

The graft is left in place about three weeks. Then the tube is opened out by making a transverse incision

Fig. 3.—Large defect after fibrous tissue has been removed at the site of the pedicle graft.

through all the tissues between the tube and the ventral surface of the penis (fig. 1 *D*). The raw edges are sutured and the penis is bandaged in hyperextension

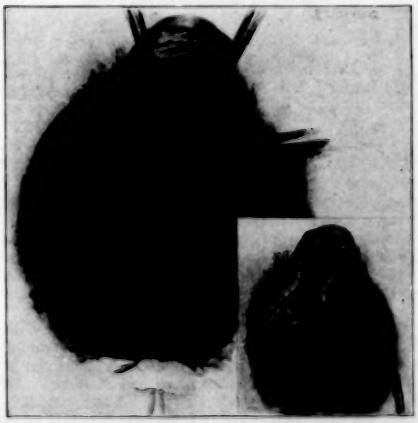


Fig. 4.—Pedicle graft swung in place and sutured.

and kept so until healing is complete. When these tunnels are opened the fibrous cord is cut and an epithelized area equal in length to the circumference of the tube is added to the ventral surface of the penis (fig. 1 *E*). All of our cases in which the tunnel graft technic

was employed were successful except one. In that case three grafts were used. One sloughed out to such an extent that it was necessary to put in another graft.

PEDICLE GRAFT TECHNIC

Because of the multiple operations sometimes necessary we devised a new technic; at least it was new to us. A transverse incision was made on the ventral surface of the penis and the contracted fibrous tissue was carefully dissected out down to the corpora cavernosa (fig. 2). This left a large skin defect about 2.5 cm. wide by 2 cm. in length (fig. 3). This was a rather large area to cover by drawing the skin together from the sides as in the classic method which is advocated by almost every author except Hagner and Smith. Large tension relieving Heineke-Mikulicz incisions would be necessary on the dorsum of the penis, and these would shorten the foreskin so much as to make it practically worthless later as a source of skin during the urethral construction, when it is most valuable. To cover the defect in this case we raised a pedicled flap from the scrotum and swung it into position over the defect, where it was fastened in place by means of skin clips (fig. 4).

This technic has been successful every time I have used it. I have had one case since in which I reverted to the Hagner technic. The contracted fibrous tissue extended so deeply and seemed so firmly attached to the corpora cavernosa that I feared it would be impossible to dissect it free without too much injury to the corpora. I used the tubular grafts instead. Even when these have to be put through the corpora cavernosa themselves there are no bad after effects that I have seen.

In bringing the pedicle graft from the scrotum, as previously described, it is simple to make the graft wide enough so that the skin may be used in building the new urethra, as described by Smith.

The pedicle graft in my hands has been more simple and has required less hospitalization for the patient than any other technic I have used. The hospital stay is reduced to eight or ten days at the most.

RECONSTRUCTION OF THE URETHRA

As stated at the beginning of this paper, it is not my purpose to dwell on this aspect of the problem of reconstruction of the urethra but merely to emphasize a few points which I have found most important.

The correction of the curvature should always be done first and a sufficient length of time allowed to intervene before any work is done on the urethra. This is necessary to determine whether the result is satisfactory or not. If it is not, further corrective measures can be taken. Never should the urethral plastic operation be attempted at the same sitting as the correction of the curvature. What appears to be an adequate correction of the curvature at the operating table may prove afterward to be wofully inadequate. Also it has happened that surgeons purposely avoided correcting the curvature because in so doing the urethral deformity would be increased and the urethral reconstruction made more difficult. A urethral meatus that is 2 cm. from the glans in the hypospadic penis may be 4 or 5 cm. from the glans after the curvature is corrected. Obviously, such an attitude is inexcusable and should be heartily condemned.

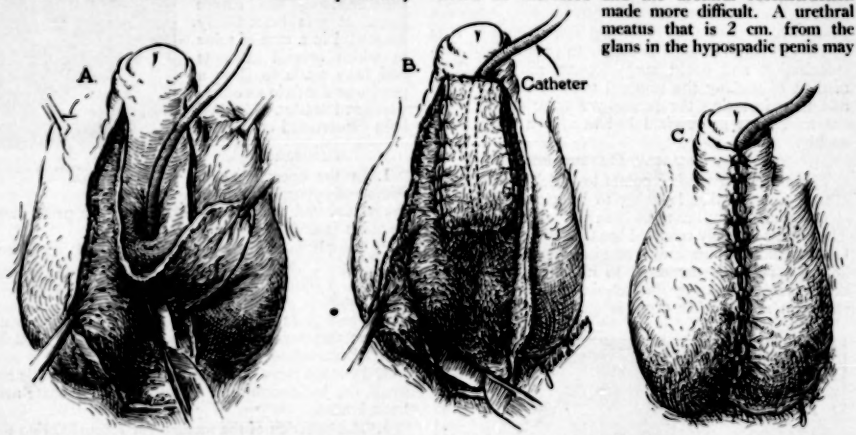


Fig. 3.—Stages in urethral reconstruction using a perineal flap to form the urethral floor.

DIVERSION OF THE URINARY STREAM

Diversion of the urinary stream, except by catheter in the immediate postoperative period, is not necessary during the operation for correction of the curvature. Any attempt at urethral reconstruction requires urinary diversion as an essential preliminary. I believe that suprapubic cystostomy is preferable in most cases because with it no urine gets beyond the internal sphincter into the urethra. There is no tube in the posterior urethra to cause the inevitable catheter urethritis and the possibility of contamination of the operative field with the resulting secretions or urine leaking around the tube. I have not tried Young's method of ligation of the bulbous urethra distal to the urethrotomy but I would expect it to be followed by stricture.

URETHRAL RECONSTRUCTION OPERATIONS

The number of different operations for the construction of the urethra is enormous. Which one is best suited in any certain case depends on the extent of the

V 113
1939

urethral defect, the condition of the available tissues and the experience of the operator with the different methods. In the balanic type the foreskin may be buttonholed and is an excellent source of skin either for construction of the urethra or for covering of bare surfaces. In the penile type if the urethra is not too far back the foreskin is again available. The Ombrédanne operation is probably the most foolproof in the less severe penile types but has the objection of giving a bulbous rather than a tubular urethra and a much less satisfactory cosmetic result. In the perineal type I have used the method of Crabtree, in which the roof of the urethra is formed of penile skin and the floor of the proximal segment of the urethra is formed of a flap of skin from the perineum posterior to the meatus (fig. 5). A foreskin flap can be used to aid in building the distal segment. One should not try to make flaps too long. Recently I attempted correction of a cleft scrotum and made the perineal flap too long, with the result that a portion of the distal end sloughed. It is better to make the flaps in stages to permit good vascularization and avoid such occurrences. Lowsley's method of making the urethral tube in the perineum and then fastening the penis over it before severing the tube from its original bed assures a good blood supply.

HAIR FOLLICLE DESTRUCTION

There are a few other points to which I would call attention. Skin that is going to be used in the construction of the urethra must have all the hair destroyed. This means not only removed but the follicles destroyed. Older authors recommended surgical removal of the follicles. I refer all my cases to a dermatologist, who destroys the follicles by electrolysis. An interval should elapse to see whether there is any regrowth or new growth and if so that too must be destroyed. A perfectly formed urethral tube can be a constant source of annoyance if hair inside is constantly becoming encrusted.

Fig. 6.—End result in case of perineal hypospadias.

THE USE OF SKIN CLIPS

Another point seldom emphasized is the use of skin clips on all external suture lines, especially in the urethral reconstruction. They do not have a tendency to cut through as do fine sutures if much edema occurs. They do not penetrate the skin and therefore do not leave a tract to predispose to the formation of fistulas. Truly enough, they do not hold as well as sutures under tension, but in urethral plastic work there should be no tension. Tension is an invitation to failure.

PEDICLE FLAPS IN CLOSING FISTULAS

Despite all care, small fistulas will sometimes occur to mar an otherwise excellent result. They may defy repeated attempts at closure because the thinness of the tissues prevents suturing in more than two immediately adjacent layers with superimposed suture lines. In these cases, after the defect is closed in the urethral lining a pedicled flap from the scrotum can be used to cover the bare area. This prevents superimposing the suture lines. It was immediately successful in a case of mine in which several attempts had been made to close a persistent fistula in an otherwise good urethra which had been constructed elsewhere.

Fig. 7.—End result in case of penile hypospadias.

SUMMARY

1. In the operative correction of hypospadias, both the sexual and the urinary function of the penis must be given consideration.

2. Complete correction of the ventral curvature should precede any attempt to reconstruct a new urethra. Failure to do this may render valueless all later work.

3. The age at which this work is done depends on the size and development of the genitalia and must be decided individually in each case.

4. In those cases in which the scrotum and penis are small, the judicious use of testosterone propionate may be indicated.

5. The selection of the method for reconstructing the urethra depends on the conditions present. There is no "best" operation for all cases.

6. Diversion of the urinary stream, preferably by suprapubic cystostomy, should precede any attempt at urethral reconstruction.

7. Skin clips are preferable to sutures in all external lines of closure.

8. All hair follicles must be completely destroyed in those areas of skin used to form the urethral tube.

9. Tension must be absolutely avoided in all plastic procedures.

25 East Washington Street.

ABSTRACT OF DISCUSSION

Dr. Clinton K. Smith, Kansas City, Mo.: The correction of the deformity seems such an obvious procedure that one wonders why it has received so little attention. I strongly suspect that the more fascinating part of the procedure, the plastic formation of a urethra, has overshadowed the less spectacular but nevertheless more important job of correcting the deformity. I should like to emphasize the importance of making an initial success of each successive step of the procedure. For instance, if a surgeon finds it necessary to reoperate to get sufficient correction of the deformity, he finds himself handicapped by the formation of scar tissue, which complicates the situation. I think that in this respect an overcorrection at the

time of the first sitting probably is one of the best forms of insurance. I like to have available at that time prepared skin grafts in order that, if it becomes necessary to denude the ventral penile surface, I can proceed with confidence, knowing that available material is at hand to cover the defect. These flaps should be attached without tension. In some of my earlier cases I had some discouraging experiences with sloughing skin grafts. I naturally fell into a plan of preparing skin grafts. This is done by taking up a section of skin on the scrotum or the foreskin and making a tube of it, allowing it to vascularize, and then later on detaching one end by slow constriction with a small rubber band. After the skin graft has been seasoned in this manner it can be manipulated with impunity, and one is practically 100 per cent certain that the graft is going to stick. There is one other point and that is the matter of the urethral opening, which is often of pinpoint caliber. This should be enlarged at the beginning and kept enlarged during the process, because in my experience the small opening, if left small, is productive of difficulty in the passing of sounds afterward.

DR. VINCENT J. O'CONOR, Chicago: The important point in the whole subject of hypospadias is rarely if ever mentioned. This is the necessity for proper correction of the penile deformity; as urologists, and therefore consultants in sexual matters, we see many persons who come to maturity with good plastic urethral construction but with an erect penile deformity which prevents intromission. It has occurred to me that the surgeon who performed the original corrective measure was either not aware of the importance of straightening the penis prior to remaking the urethra or else was interested only in the position of the urethral meatus. In my private practice I have seen sixteen patients who had so much penile deformity after a good reconstruction of the urethra done elsewhere that marriage was impossible. The severe deformities in these cases are the result of a thickening in the floor of Buck's fascia, and a simple dissection which merely frees the corpora cavernosa, as practiced by most surgeons, does not correct the deformity. The Hagner tunnel graft, which is placed directly through the corpora and permits ultimate incision of the thickened fascia, is the only method that will result in a correction of the severe type of deformity. As urologists who more keenly appreciate this problem, we should emphasize this most important point to those who operate on young boys at an age when this problem is not so apparent.

DR. VILRAY P. BLAIR, St. Louis: The principles of the plan that I have used for thirty years and modified from time to time contemplate three separate operative steps, or more when needed. The principles underlying the plan are: 1. (*a*) Release of the ventral or dorsal shortening by painstaking dissection and removal of the fibrous sheet that is closely adherent to the corpora cavernosa, the traction of which causes ventral bowing in the hypospadias or total shortening and weakened action of the vesical sphincter in the epispadias. (*b*) Immediate ample coverage of the resulting raw area with tissue drawn mesially from the body of the penis and pedicle flaps from the prepuce. It is from this covering that the lining of the new urethra will be constructed at the second step. 2. (*a*) Construction of the missing section of the pendulous urethra, either to the frenum or to the tip of the glans over a section of soft catheter of a size proportionate to the patient's age. (*b*) The resulting raw surface is immediately covered by a scrotal flap with a base much wider than its length. 3. The base of the scrotal flap is cut free, and the still remaining scrotal part of the urethral defect is closed. If done carefully on a patient who has not been circumcised, this procedure will give an anatomic restoration which is close to normal excepting that the new urethra will not be fixed to the corpora cavernosa. I believe that successful healing will depend largely on the following essentials: 1. Control of all bleeding by triple 0 silk ties. 2. Carefully placed superimposed deep and superficial rows of fine silk sutures in each suture line that insure deep approximation of flap edges. 3. Avoidance of superimposed suture lines. 4. Drainage by an indwelling catheter. I have discarded both cystostomy and urethrostomy in favor of indwelling catheter drainage, which I have found on the average to be the least of three evils. I prefer that the latter remain in place from five to ten days. This is particularly desirable when the same catheter also supports the newly sutured urethra. 5. Choice of dressings. I rely chiefly on snug double spica-bandaged pressure dressings which splint the penis firmly against the abdomen or perineum to prevent accumulations of blood and control both infection and priapism, using gauze for wound protection and moist sea sponges for padding pressure. 6. Age of patient at operation. For the psychology of parents and patients I consider it a distinct advantage to complete the repair before puberty and have succeeded in doing this as early as 7 years. The hospitalization for the first step will average around one week and for the second and third steps, which are done with a minimum of an interval of three weeks, between ten and fourteen days each. An indefinite period elapses between the first and the second step.

DR. FREDERIC E. B. FOLEY, St. Paul: I will discuss only the problem of reconstructing the urethra. For many years I fussed with all the trick flaps, hair-bearing skin, prepuce and scrotum familiar to all of us. This was attended by all the difficulties referred to in Dr. McKenna's paper and in the previous discussion. Almost invariably it was a matter of four or five procedures, secondary closures of little fistulas, hair growing in the new urethra and so on. My results corresponded fairly well to other results and photographs which I have seen but not to the illustrator's drawings. For me the whole enterprise was beset with difficulty, and it was not a gratifying experience. A year ago Virgil Counseller called my attention to McIndoe's operation—a modification of the tube inlay graft of Nové-Josserand. I was aware of the original Nové-Josserand operation and of the fact that it gave very poor results owing to contraction and cicatrization of the inlay tube graft. McIndoe avoids this difficulty by keeping a removable mandril in the transplanted skin tube for several months. I tried the method. It has been a very gratifying experience. The operation for correcting the ventral curvature deformity should be done at an early age and repeated until a straight penis is obtained. The plastic operation to form the urethra must not be done until the penis is of near adult size. A special instrument is required. It consists of a metal tube size F. 24 and 10 or 12 cm. long. To one end of the tube is screwed a solid spear-pointed end; to the other end is screwed a handle. The spear-pointed end is pushed along under the skin of the ventral surface of the penis from the hypospadiac meatus to the glans, where it emerges in the position of a normal meatus. The spear-pointed end and handle are then unscrewed, the metal tube being left in the position of the new urethra. A thin sheet of skin cut from a non-hair bearing surface is wrapped around a catheter of size F. 20 or F. 22—"butter side out" of course—and is held in place with ties. This tube graft carried on the catheter is passed into the metal tube to the appropriate position. The metal tube is then withdrawn over the catheter, the tube graft being left in the grip of the surrounding structures. Ten days later the catheter is removed, the transplanted skin tube being left in place as a new urethra. For from eight to ten months the patient must wear an obturator in the newly formed urethra to prevent its contraction. A segment of soft rubber catheter serves this purpose well and causes no discomfort. At the end of this period the procedure is completed by anastomosing the hypospadiac meatus with the proximal end of the tube graft. By this method I have obtained by far the best result.

DR. CHARLES M. MCKENNA, Chicago: The majority of patients suffering with hypospadias will sooner or later have an inferiority complex. This is usually true in any deformity of the genital organs. The patient should be encouraged rather than discouraged. Surgeons doing this type of work must be prepared for some grief, since the result will not be perfect in all cases. I think this should be explained to the family so that the impossible will not be expected in one sitting. Careful attention should be given to the blood supply to make a good result possible. When a graft is being made all tension should be relieved so that slough may be prevented. The technic is not the same on all patients. In other words, the fundamentals will be used but the technic will vary according to the type of deformity which confronts the surgeon.

Clinical Notes, Suggestions and New Instruments

STUDY OF A MALE CASTRATE

LAURENT FEINIER, M.D., AND THEODORE ROTHMAN, M.D., NEW YORK

Despite published evidence to the contrary, a rather common belief persists that complete castration of the adult male results in impotence.

For many years it has been known that the sexual impulse tends to continue in animals after castration. Sexual instinct and potency often persist in the ox and the gelding.

Havelock Ellis [1] reported that many castrated men continued to possess sexual impulses, as noted by medical observers in countries where eunuchism was produced and eunuchs were employed. McCartney [2] reported that ten of the twenty-three eunuchs examined by him showed gonorrhea. Osman and Schukru [3] reported the continuation of sexual instincts and successful efforts in eunuchs. The earlier the age at which castration is performed the less marked the subsequent sexual desire, and the Chinese regarded boys castrated before the age of 10 as particularly pure and virginal.

Lange [4] reviewed more than 300 cases of soldiers who had been castrated during the World War as a result of bullet wounds or tuberculosis. Of the 220 who were unmarried at the time of castration, 155 have married and "not a few did not notice any impairment of libido for many years and potency remained for a long time, although in a generally decreasing way." Kolle [5] reported a series of fifty-eight surgically castrated men in at least a third of whom libido and potency appeared to be preserved. In contrast are the reports of de Quervain and Wolf [5] at Berne and of Goll [5] in Denmark, who reported consistent and almost entire suppression of libido and potency. The report from Berlin that a large proportion (possibly 30 to 50 per cent) of castrated criminals previously guilty of sexual offenses did not become repeaters is obviously open to psychiatric interpretation rather than complete acceptance on the basis of physical and hormonal mechanisms. Rowe and Lawrence [6] reported a case of successful mental readjustment and sexual success in a surgically castrated man 25 years of age, whereas McCullagh and Renshaw [7] reported loss of libido in nine of twelve adult male castrates.

Not unrarely, patients suffering from certain mental diseases seek and even demand castration and after the procedure may derive some temporary relief from mental conflicts and anxieties. Unwise and hazardous as such therapeutic procedure usually is, it is somewhat surprising to discover how frequently it has been rationalized and recommended by physicians. As Menninger [8] has described, castration is even comparatively recently reported in the *Quarterly Cumulative Index Medicus* as a possible form of therapy for neurosis, perversions and sexual abnormalities, sexual crimes, mental diseases and tuberculosis.

The overemphasis which has been placed for so long on the gonads as the main source of potency and libido in males is certainly not in accord with general medical knowledge concerning female castrates, who so often after surgical or x-ray procedure retain complete libido and ability for sexual responses.

Following is a report of long retention of sexual prowess in a surgically castrated man:

REPORT OF CASE

History.—A. I., aged 53, was admitted to the Vanderbilt Clinic because of severe periodic headaches occurring from twice a week to once a month, usually confined to one side of the head but often bitemporal and frontal and usually lasting from twelve to forty-eight hours. Either during or after the headaches, the patient was usually nauseated and vomited. The onset occurred thirty years previously, three to four months after complete orchidectomy for gonadal tuberculosis. One testicle was removed in a New York hospital and a few months later the other was removed in Naples, Italy.

At 7 years of age the patient had a convulsion without known cause. In the next year and a half several other seizures occurred, following which there was no further recurrence. He was considered a "weak and sickly" child.

The patient's mother suffered headaches of a type similar to his own. A sister was operated on for trigeminal neuralgia. His maternal grandmother became psychotic during the latter part of her life.

Previous to the surgical castration thirty years before, the patient had sexual intercourse about once a month and considered his potency and prowess rather poor. Nevertheless, three children were born. Subsequent to the removal of the second testicle his libido and potency promptly became definitely increased and in the words of his wife, to whom he had been married four years, "he was like a newly married man." The patient stated that thereafter he enjoyed his marital relationship more thoroughly and robustly until the past six months, during which the periodic headaches became more severe and more frequent and he had intercourse about once a week. There was no ejaculation other than a "few drops of sticky fluid."

Physical Examination.—The patient was well nourished, weighing 179 pounds (81 Kg.), cooperative and fairly intelligent. The habitus was feminine, with increased fat distributed about the breasts, hips and abdomen. The mammary areas were definitely enlarged. Pubic hair distribution was of the feminine type. The eyebrows were rather heavy and prominent. There was no evidence of testicular tissue. The voice was soft and modulated. The patient was polite, modest and courteous, with at times a suggestion of effeminate mannerisms.

There was no evidence of organic involvement of the nervous system, mouth, heart, lungs or abdomen.

The genito-urinary consultant was Dr. Leonard Hallock. He found no testicular tissue. The prostate as felt by rectum was very small and flat, not unlike many prostates in normal persons with normal testicles. The evidence of atrophy of the prostate was in accord with the cases reported by McCullagh and Renshaw, as was also the comparatively normal size of the penis.

The endocrine consultant was Dr. Irving Pardee. The skin was smooth with a slightly yellowish tinge. It presented a scanty line of hair on being stroked. The hair growth throughout was scanty; a beard was present but not profuse. Pubic hair was transverse and scanty. There was no mammary development, only fat. There was no structural change in the body or change in the voice. Dr. Pardee stated that the retention of libido is not unusual in these cases; as it had been reported in the literature and seen in one of his cases. He held that the headaches in the present case were characteristically pituitary in type and location, being bitemporal and frontal. Their onset after orchidectomy and the undoubted "prolan of castration" and its counterpart in the castration cells of the pituitary linked up this syndrome.

Laboratory Examination.—The blood count was normal. Blood chemistry showed a urea nitrogen level of 11.4 mg., urea 24.4 mg. and sugar 96 mg. per hundred cubic centimeters.

From the Neurological Department of the Vanderbilt Clinic and the Neurological Institute of New York, service of Dr. Henry A. Riley.

1. Ellis, Havelock: Studies in the Psychology of Sex, Philadelphia, F. A. Davis Company, 1901-1931.
2. McCartney, J. L.: Dementia Praecox as Endocrinopathy with Clinical and Autopsy Reports, Endocrinology **13**: 73-87 (Jan.-Feb.) 1929.
3. Osman, Mazhar, and Schukru, Ihsan: Les eunuques: Etude anatomo-clinique et anthropologique, Hyg. ment. **31**: 33-45 (Feb.) 1936.
4. Lange, J.: Kastration vom Standpunkt des Psychiaters, Med. Klin. **30**: 1081-1084 (Aug. 17) 1934.
5. Problems of Heredity, Berlin letter, J. A. M. A. **103**: 1051-1052 (Sept. 28) 1935.
6. Rowe, A. W., and Lawrence, S. H.: Studies of Endocrine Glands; Male and Female Gonads, Endocrinology **12**: 591-662 (Sept.-Oct.) 1928.
7. McCullagh, E. P., and Renshaw, J. F.: Effects of Castration in Adult Male, J. A. M. A. **103**: 1140-1143 (Oct. 13) 1934.
8. Menninger, K. A.: Polysurgery and Polysurgical Addiction, Psychoanalyt. Quart. **3**: 173-199 (April) 1934.

The Wassermann reaction of the blood was negative. The dextrose tolerance values were 92, 102, 82, 96, 102, 112 and 62 mg. The basal metabolic rate, determined on three different occasions, was — 13, — 10 and — 20 per cent.

The determination of the gonad stimulating factor called "prolan" was 4 plus on two occasions and subsequently negative on two occasions.

Dr. Hugh H. Darby of the Department of Biological Chemistry, Columbia University College of Physicians and Surgeons, found no evidence in the patient's urine of the presence of either testosterone or androsterone. The extract and concentrate from 3,000 cc. of the urine when injected into capons produced no comb growth.

X-ray examination showed a normal skull. The sella turcica did not show any abnormalities.

Psychologic and Neurologic Examination.—The Arthur tests showed that the patient's intelligence quotient was 80. His English vocabulary and educational background were limited. Responses to the Rorschach ink blots suggested a reasonably good intellectual endowment and a neurotic tendency.

Masculinity-femininity tests (Terman and Miles [9]) resulted in a suggestion of a slightly feminine type, but the trend was not considered significant, the patient's reactions being standardized at the more feminine end of the masculine range.

Some degree of neuropsychiatric hereditary background was noted in the family history. The patient was one of ten children and in childhood was apparently overprotected by too solicitous parents. As a result of his convulsive seizures he was refused admission to school and keenly felt his social isolation and situation of insecurity. At puberty he began autoerotic practices, which were continued through late adolescence. Later, minor difficulties were experienced in adjustment to work and to social life. His courtship and marriage were apparently normal and, although the subsequent weakness in heterosexual relationship might be interpreted as a result of neurotic mechanisms, it could be attributed to the tuberculosis of the testicles. Preoperatively the patient had considerable fear of castration. He had been told that complete loss of virility would result. However, he had a strong erection on the fourth day after the removal of his second testicle. His continued potency and the gain in weight, although the latter was largely contributed to by increased adiposity around his breasts and pelvic girdle, was followed by his explanation that he "was stronger and more of a man than ever before."

During hospitalization no discrepancies in his ward conduct were noted. He was affable, showed considerable innate intelligence, had a good sense of humor and showed considerable pride in his one time association as secretary to a famous male singer. His behavior showed none of the profound mental changes which Rowe [10] has reported may occur in male castrates.

COMMENT

The rather abrupt increase in sexual activity and prowess in this patient following castration was probably favorably influenced to some extent by the removal of the tuberculous foci.

It is possible that a compensatory Don Juan reaction to a castration fear in a person of a neurotic type might have played a secondary part in his sexual rejuvenation, but it is believed that the patient's increase in libido and potency was a compensatory mechanism in his unconscious for his castration. Psychically he gained something because of the loss of his testicles. He believed that he had grown heavier and therefore stronger and had proved he was more of a man. This obviously was a form of rationalization on the patient's part, although the favorable physical and psychic results following the removal of the tuberculous foci can by no means be entirely discounted in attempting an interpretation of his subsequent reactions. Subsequently his position as secretary to a famous singer served to improve and maintain his morale. In psychiatric summary, this patient resembled the six patients with eunuchoidism studied by Carmichael and Kenyon [11] in that he did not reveal any characteristic mental picture, which is in accord with the opinion of Löwenthal [12] (as mentioned by these authors) that the sexual defect is the one feature which eunuchoids share in common. It would appear that adult castrates may vary as widely in their personal reactions and mental adjustment to orchidectomy as do people in general to the various other difficulties in life.

The development of physical characteristics suggestive of eunuchism appeared directly dependent on the castration, the resultant lack of testis hormone or hormones and the subsequent endocrine imbalance. Admitting the possibility that there may have been some testis or testis-like hormone in the patient's food supply, the capon tests for male hormones gave negative results. Although he was not castrated until 23 years of age the patient's physique supports the view that adequate gonadal activity is not only necessary for reproductive function but may also, even as comparatively late as young adulthood, be necessary for the complete development and the full maintenance of normal physical characteristics.

The rather low basal metabolic rates are in accord with pathologic-anatomic data reported by Wagenseil [13] and the reports on eunuchoids by Carmichael and Kenyon [11] and on castrates by McCullagh and Renshaw.[7]

Although the patient's mother suffered periodic headaches of a type somewhat similar to his own, the onset a few months after castration in this case supported an interpretation that he suffered a lack of gonadal secretion and its inhibitory effect on the anterior pituitary. The gonadotropic substance found on several occasions and the bitemporal and frontal location of the headaches also confirmed the indictment of the pituitary gland as a factor.

The therapeutic response to ergotamine tartrate and phenobarbital was satisfactory, with no occurrence of severe headache for three weeks, whereas before admission he had been having a severe attack about twice a week.

The patient's conduct and behavior reactions, although slightly suggestive of the feminine type, were not sufficiently so to permit any definite deductions or conclusions. His emotional instability and neurotic tendency appeared as a result of his sickly childhood and the overprotection he received from a too solicitous mother.

This case is of interest in connection with the reports in the literature which have described the therapeutic use and value of testicular extracts in male adult impotence. It suggests that such beneficial effects are the probable result of either a gonadal suppressive action on the pituitary or, in some instances, a favorable psychogenic reaction.

It appears that in the full-grown adult the only indispensable sexual function of the testes is that of procreation and that libido and potency are functions of and controlled by the prepituitary and the psychic centers.

After puberty and adolescence with the development of the male sexual characteristics, castration need not result in the loss of libido and potency, nor are prominent mental or physical changes a necessary aftermath. Retention of sexual power probably depends to a considerable extent on the subject's preoperative mental characteristics, type of personality pattern and tendency either to resign himself passively to his sexual defect or else combatively to compensate for it. Neuropsychiatric supervision of these cases should be of considerable value in

9. Terman, L. M., and Miles, C. C.: Sex and Personality: Studies in Masculinity and Femininity, New York and London, McGraw-Hill Book Company, 1936.

10. Rowe, A. W.: Studies of Endocrine Glands: Differential Diagnosis of Endocrine Disorders, Endocrinology **13**: 327-362 (July-Aug.) 1929.

11. Carmichael, H. T., and Kenyon, A. T.: Eunuchoidism: A Psychiatric and Endocrine Study of Six Cases, Arch. Neurol. & Psychiat. **40**: 717-742 (Oct.) 1938.

12. Löwenthal, Karl: Der Eunuchoidismus des Mannes, Beitr. z. path. Anat. u. z. allg. Path. **80**: 426-439, 1931.

13. Wagenseil, Ferdinand: Beiträge zur Kenntnis der Kastrationsfolgen und des Eunuchoidismus beim Mann, Ztschr. f. Morphol. u. Anthropol. **26**: 264-304, 1927.

directing the patient's mental readjustment to castration, and it is suggested that when possible such psychotherapy should be instituted preoperatively.

SUMMARY

A 53 year old surgically castrated man retained libido and prowess for thirty years after complete orchidectomy. The patient's physical habitus suggested the feminine distribution of fat and pubic hair. No physical change was noted in the size or appearance of the penis. Tests for testosterone and androsterone gave negative results. Shortly after castration, migraine attacks began and continued, being of a type and character suggesting an unbalanced pituitary hyperfunction.

706 West 168th Street.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

METAPHEN (See New and Nonofficial Remedies, 1939, page 328).

The following dosage form has been accepted:

Medipax Brand of Vaginal Tampon-Suppositories with Metaphen 1:2,000: A product devised to enable prolonged medication to the upper vaginal vault and cervical region by incorporating a metaphen medicated suppository together with a tampon on a single applicator.

Actions and Uses.—The suppository contains 2.25 mg. (0.0375 grain) of metaphen in 4.5 Gm. (75 grains) of glycerogelatin shaped for insertion. After insertion into the vagina the suppository melts at body temperature. The tampon which is contained in the applicator and is composed of surgical cotton 1¾ inches wide by 2¾ inches long is released by appropriate pressure on the sleeve of the applicator. The tampon swells by taking up moisture, thus holding the medication in contact with the desired parts. A cord is attached to the tampon for convenient removal.

Prepared by Allen Laboratories, Inc., New Brunswick, N. J.

MERTHIOLATE (See New and Nonofficial Remedies, 1939, p. 326).

The following dosage form has been accepted:

Medipax Brand of Vaginal Tampon-Suppositories with Merthiolate 1:2,000: A product devised to enable prolonged medication to the upper vaginal vault and cervical region by incorporating a merthiolate medicated suppository together with a tampon on a single applicator.

Actions and Uses.—The suppository contains 2.25 mg. (0.0375 grain) of merthiolate in 4.5 Gm. (75 grains) of glycerogelatin shaped for insertion. After insertion into the vagina the suppository melts at body temperature. The tampon, which is contained in the applicator and is composed of surgical cotton 1¾ inches wide by 2¾ inches long, is released by appropriate pressure on the sleeve of the applicator. The tampon swells by taking up moisture, thus holding the medication in contact with the desired parts. A cord is attached to the tampon for convenient removal.

Prepared by Allen Laboratories, Inc., New Brunswick, N. J.

BISMUTH SUBSALICYLATE (See New and Nonofficial Remedies, 1939, p. 141).

The following dosage form has been accepted:

Ampuls Bismuth Subsalicylate in Oil 0.13 Gm. (2 grains), 1 cc.: Each cubic centimeter contains bismuth subsalicylate-U. S. P. 0.13 Gm. (2 grains) in sterile olive oil suspension containing 3 per cent chlorobutanol (chloroform derivative).

Prepared by the William S. Merrell Company, Cincinnati, Ohio. No U. S. patent or trademark.

LUMINAL SODIUM (See New and Nonofficial Remedies, 1939, p. 126).

The following dosage form has been accepted:

Luminal-Sodium Tablets, 1 grain.

MERCURIC SALICYLATE (See New and Nonofficial Remedies, 1939, p. 319).

The following dosage forms have been accepted:

Ampuls Mercury Salicylate in Oil 0.065 Gm. (1 grain), 1 cc.: Each cubic centimeter contains mercuric salicylate-U. S. P. 0.065 Gm. (1 grain) in sterile olive oil suspension containing 0.5 per cent quinine and urea hydrochloride-U. S. P.

Prepared by the William S. Merrell Company, Cincinnati, Ohio. No U. S. patent or trademark.

Ampuls Mercury Salicylate in Oil 0.1 Gm. (1½ grains), 1 cc.: Each cubic centimeter contains mercuric salicylate-U. S. P. 0.1 Gm. (1½ grains) in sterile olive oil suspension containing 0.5 per cent quinine and urea hydrochloride-U. S. P.

Prepared by the William S. Merrell Company, Cincinnati, Ohio. No U. S. patent or trademark.

Council on Foods

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT BY DR. COWGILL OF ONE OF THE TOPICS DISCUSSED WHEN CONSIDERATION WAS BEING GIVEN TO THE QUESTION OF THE DESIRABILITY OF ADDING VITAMIN B_1 TO FOODS. PARTLY ON THE BASIS OF THIS REPORT, THE COUNCIL HAS ADOPTED CERTAIN POLICIES WHICH HAVE BEEN REPORTED IN THE JOURNAL FOR AUG. 19, 1939.

FRANKLIN C. BING, Secretary.

THE NEED FOR THE ADDITION OF VITAMIN B_1 TO STAPLE AMERICAN FOODS

GEORGE R. COWGILL, PH.D.

NEW HAVEN, CONN.

The recent isolation and synthesis of vitamin B_1 (thiamin) [1] has placed in the hands of clinicians and students of nutrition alike a most valuable therapeutic agent as well as dietary essential in pure form. Clinical trial of this substance in the United States over a comparatively short period has already yielded results so striking as to warrant consideration of the question of the adequacy of American dietaries with respect to vitamin B_1. It has been generally recognized that the dietaries in common use in the Orient and certain other parts of the world where beriberi is endemic are seriously deficient in this factor, but until comparatively recently it has been questioned whether this is true also for the United States and European countries. The recent and remarkable successes attending the use of pure vitamin B_1, often in conditions in which lack of this factor seemed quite unlikely, can be interpreted only as meaning that vitamin B_1 deficiency must be much more widespread in this country than clinicians have believed hitherto. Strauss,[2] who has reviewed this recent therapeutic use of vitamin B_1, definitely states that "vitamin B_1 deficiency is probably more commonly found in the United States than has been supposed. The observations of Spies and his colleagues,[3] who have been studying pellagra, are particularly interesting in this connection. In many of their cases in which nicotinic acid has been provided but the patients allowed to continue on their customary diets the symptoms of pellagra have been relieved but those of beriberi have eventually appeared, thus demonstrating the presence of a B_1 deficiency masked by a more serious shortage of nicotinic acid. Jolliffe [4] has recently published a clinical evaluation of the adequacy of vitamin B_1 in the American diet. He concludes that the margin of safety against beriberi afforded by American dietaries "varies from 20 to 80 per cent," depending on the method used in making the evaluation. "A large fraction of our population, particularly those spending per capita less than two dollars per week for food, subsist on diets of borderline adequacy in vitamin B_1." Jolliffe also expresses the opinion that, "while vitamin B_1 deficiency is endemic in the United States, this disease, called beriberi in the Orient, is usually classified here under one of a variety of misleading diagnoses such as 'alcoholic,' 'gestational,' 'diabetic,' 'metabolic,' or 'gastrogenous' polyneuritis" (p. 65).

From the Laboratory of Physiological Chemistry, Yale University.

1. Williams, R. R.: The Chemistry of Thiamin (Vitamin B_1), J. A. M. A. **110**:727-732 (March 5) 1938.
2. Strauss, M. B.: The Therapeutic Use of Vitamin B_1 in Polyneuritis and Cardiovascular Conditions, J. A. M. A. **110**:953 (March 26) 1938.
3. Spies, T. D., and Aring, C. D.: The Effect of Vitamin B_1 on the Peripheral Neuritis of Pellagra, J. A. M. A. **110**:1081-1084 (April 2) 1938. Also personal communication to the author from Dr. Spies.
4. Jolliffe, Norman: A Clinical Evaluation of the Adequacy of Vitamin B_1 in the American Diet, Internat. Clin. **4**:46-66 (Dec.) 1938.

To students of the physiology of vitamin B_1[5] these recent developments are by no means unexpected. The relation of minimum daily requirement to effective curative dose in animals, considered along with such estimations of the probable human requirement as it was possible to make in the absence of trials with the pure vitamin, suggested that with the concentrates available at the time it would be very difficult to demonstrate in any dramatic fashion the value of this vitamin in the treatment and prevention of the less striking features of the beriberi picture. Conservative interpretation of such clinical observations as were made with vitamin concentrates was doubtless to be expected.

The recent changing view of clinicians regarding the serious probability of vitamin B_1 deficiency in this country raises some interesting questions for all students of nutrition and public health. The solution of these questions is of great importance in relation to the general health and welfare of our people.

Let us first consider how much vitamin B_1 human beings should receive. From the data presented in a recent review of the literature bearing on this question[6] it appears that adults require daily as a minimum approximately 300 to 350 international units (I. U.) of the vitamin, which is equivalent to about 1 mg. of the pure thiamin.[7] This minimum is equal to about 10 international units per hundred calories daily. Preschool children apparently need as much as 20 to 25 or more international units per hundred calories daily. It is pertinent to consider to what extent these requirements are being met under the dietary conditions prevailing in the United States. If they are being met, what appears to be the factor of safety above these minima afforded by our American dietaries?

FOOD STATISTICS

In attempting to answer these questions, statistics of food consumption for the nation as a whole may be examined, particular attention being paid to those foods which are low in vitamin B_1 but used in relatively large amounts. The two most important foodstuffs in this connection are the cereals, with their refined products, and sugar.

Cereals constitute the principal source of energy in the world's diet, but the predominance of particular cereals over others in any given part of the world appears to be the resultant of a variety of factors, notably ease of cultivation, cost, purchasing power of the population, custom and taste. As is well known, rice is the staple cereal in the Far East, whereas wheat occupies the dominant position in the United States and Europe. For the years just before the Great War, it appears that the people of the United States secured about 34 per cent of their total calories from cereals; 26 per cent were derived from wheat, which constituted about 75 per cent of the total cereals used.[8]

In table 1 are presented data for consumption of wheat in the United States during certain periods.

From the review of data on world use of cereals prepared by the Mixed Committee of the League of Nations[9] (see table 1) it is evident that there has been a steady decline in the food use of bread cereals for a period of years, and this decline appears

> to have been greatest in the countries where the great bulk of the cereal consumption consists of wheat. These are, in general, the countries with the highest levels of living; as income rose, there was a partial substitution of more expensive noncereal foods for wheat. In countries where rye or maize was the principal cereal, there has, on the other hand, been a tendency towards their displacement by wheat [p. 102].

For a person with an average daily energy exchange of 3,000 calories, the wheat consumption for 1929-1934 (table 1) would mean approximately 32 per cent of the calories derived from this cereal. Assuming that the decline in consumption of cereals in the United States has continued to the present year, it does not seem unreasonable to conclude that our population, by and large, secures probably as much as 25 per cent of its calories from wheat and its many products.

Let us consider what this means with respect to intake of vitamin B_1. The roller mill for manufacture of wheat flour was invented by Helfenberger about 1830. The first American rolls to be constructed were installed in Connecticut about 1874. Prior to Helfenberger's invention wheat flour was obtained by grinding between stones. According to Baker, Wright and Drummond[10] such a flour represented 81.4 per cent of the original wheat kernel and contained on an average 1.65 international units of vitamin B_1 per gram and about 62 per cent of the total vitamin present in the wheat. In contrast to this, modern wheat flour represents only 72.5 per cent of the kernel and has as low as 0.15 international unit of vitamin B_1 per gram and only about 5.5 per cent of the vitamin originally contained in the cereal. In other words, the modern milling process gives us a product with a vitamin B_1 content about one eleventh of that of the old stone-ground flour. Such a change would not be of much practical importance if the products in question formed only a relatively small part of the dietary. When, however, they furnish as much as 25 or more per cent of the total calories consumed, this tremendous decrease in vitamin B_1 content becomes serious indeed.

TABLE 1.—*Consumption of Wheat and Cane Sugar*

Food	Period	Consumption: Per Capita: Per Year, Kg.	Consumption: Per Capita: Per Day, Gm.	Yielding About: Calories per Day	Yielding About: Per Cent of 3,000 Calories Daily
Wheat (Wheat Studies of the Food Research Institute, Stanford University, Calif. 11, No. 7, 12, No. 10, 1935)	1904-1909	145.6	399		
	1909-1914	140.2	384		
	1929-1934	100.2	274		
Cane sugar (1921, 1850, 1900 and 1929 Nutrition,[9] p. 108, 1931, Mendel, L. B.: J. A. M. A. 80: 117 [July 9] 1923)	1821	3.6	9.9	39	1.3
	1850	12.6	37.3	149	5.0
	1900	30.2	83.8	335	11.2
	1929	47.0	128.8	515	17.2
	1931	49.0	134.2	537	17.9

Another well known component of the American dietary important in this connection is sugar. Table 1 presents data indicative of the consumption of this food in the United States over a period of years.

In contrast to the decreasing use of cereals there has been a steady rise in the consumption of the highly purified foodstuff cane sugar. No doubt this has been due in considerable measure to the great developments

5. Cowgill, G. R.: The Physiology of Vitamin B_1, J. A. M. A. 110: 803-812 (March 12) 1938.
6. Cowgill, G. R.: Human Requirements for Vitamin B_1, J. A. M. A. 111: 1009-1016 (Sept. 10) 1938.
7. The latest (1938) definition of the international unit specifies that it be equal to 3 micrograms of the pure vitamin. This means that 333 international units is contained in 1 mg. of crystalline thiamin chloride.
8. Wheat Studies of the Food Research Institute 8, No. 4: The Place of Wheat in the Diet, Stanford University, Calif., 1929.
9. Nutrition: Final Report of the Mixed Committee of the League of Nations on the Relation of Nutrition to Health, Agriculture and Economic Policy, Geneva, 1937. See p. 102 et seq.
10. Baker, A. Z.; Wright, M. D., and Drummond, J. C.: The Nutritive Value of Bread, J. Soc. Chem. Ind. 56: 191-194 (Trans.) 1937.

in the sugar industry making the available supply greater than ever before, but the sweet taste of this product has also played a great role. That sugar is valuable as a source of energy cannot be questioned, but, to the extent that it displaces other foods which may at the same time function as carriers of important nutrients such as minerals and vitamins, this increasing use of sugar is obviously not in the public interest.

The statistical data presented in table 1 indicate that the American people secure something like 42 or more per cent of their calories from these two foodstuffs relatively poor in vitamin B_1 or free of it. The decreasing use of wheat, which is a fact to be considered, cannot be regarded as playing a significant helpful role in this connection, because it is more than offset by the increasing use of sugar. In the decades immediately after the introduction of modern milling processes there was still an appreciable demand for less highly refined wheat products. However, the more refined white flour has steadily gained in popularity because of its many advantages, notably its stability in commerce as contrasted with whole wheat flour, for example, and its whiteness with consequent appeal to the eye, suggestion of greater purity. This last named advantage (?) is similar to that possessed by polished rice, which has proved to be the favored cereal in the Far East in spite of numerous governmental efforts to secure widespread substitution of undermilled rice for it in the attempt to combat beriberi.

The foregoing summary of statistics on wheat and sugar suggests that these foods supply daily at least 42 per cent of the total calories. It will be noticed that I have taken 3,000 calories a day as the base of reference. If smaller figures, 2,700 or 2,500, for example, are used, the percentages become 55 and 60, respectively. If Swanson's treatise on "Wheat and Flour Quality" [11] is taken as the authority, the total calories obtained daily per capita from wheat and cane sugar represent about 1,375 calories. This constitutes 45 per cent of a 3,000 calory total, and 51 and 55 per cent when the daily totals are 2,700 and 2,500 calories, respectively.

In commenting on the significance of these changes in food habits and the effects of milling on the wheat, Jolliffe aptly writes: "It seems, therefore, that a 55 per cent fraction of the calories in the American diet of 1840 containing a minimum of 600 I. U. of vitamin B_1 has been replaced in the contemporaneous American diet by a like fraction containing only about 50 I. U." (p. 52).

Students of nutrition now emphasize a greater use of the so-called "protective foods," which are primarily milk, green vegetables and fruits. These foods are excellent sources of calcium (milk and green vegetables) and vitamin C; however, they do not rate high in vitamin B_1 content. If the American people continue to use wheat and sugar in amounts currently consumed, simple calculation reveals that, in order to secure the 550 international units of vitamin B_1 which has been lost during the past century as a result of refinement in milling of wheat, one would be forced to consume tremendous and impossible quantities of these particular "protective foods." Taking the distribution of foods characteristic of the average American diet described by Sherman [12] as a basis of estimation, Jolliffe [4] finds that one would have to consume daily a combination of 625 Gm. of fruit, 600 Gm. of potatoes, 880 Gm. of other vegetables and 1,260 cc. of milk. This combination is, of course, impossible because of its bulk. It might be supposed that there are many other foods which could be used to advantage here, but careful study of this point indicates that these "other foods" are rather limited. Thus, an examination of the lists given on pages 236-240 in tables X-XVI of the monograph by Williams and Spies [13] indicates that only ten foods contain more than 3 micrograms of thiamin per gram of the food. In order to appreciate the significance of these figures, the reader should remember that whole wheat contains on an average about 4.6 micrograms per gram. A more liberal use of other seeds besides those of the cereal plants, notably nuts, and the members of the legume family, such as beans and peas, would constitute a partial solution of the problem. However, these foods are all of them quite concentrated with respect to energy and therefore can be used in this way only to the extent that they replace cereals and sugar. On the other hand, fruits, vegetables and milk, because of their high moisture content, must be ingested in considerable quantity in order to serve as noteworthy sources of calories. Another point is worthy of mention in this connection. Many of the foods that might be considered suffer some loss of the vitamin through poorer methods of preparation in the home, such as, for example, those which involve leaching out into the water used in cooking and then rejection of that water. The operation of this factor cannot be stated quantitatively, but obviously any consideration of it means that the public's intake of the vitamin may be even lower than the foregoing rough estimates.

The discussion thus far has been limited almost entirely to wheat and sugar, and it has been shown that no very satisfactory solution of the problem can be expected by efforts directed toward greater use of the "protective foods" other than whole grains or the germ. It seems unnecessary to belabor the point that, so far as food statistics indicate, the American dietary is not rich in vitamin B_1, as many people have supposed, but too close to the minimum in this respect to be viewed with equanimity.

AMERICAN DIETARIES

Statistical studies of food consumption such as have been discussed constitute only a first approximation answer to the question What do the people eat? More precise information must come from examination of food intake records. Fortunately, data of this sort are available for examination. Stiebeling and Phipard [14] have made extensive analyses of the content, cost and nutritive adequacy of diets of employed wage earners and low salaried clerical workers in four sections of the United States, namely North Atlantic states, Pacific, East South Central and the South:

> The study was based on about 4,000 records of a week's food consumption, placed at the disposal of the Bureau of Home Economics through the courtesy of the Cost of Living Division of the United States Bureau of Labor Statistics. The records were collected in 1934-37 as part of a study of income and disbursements for family living.

In their discussion of vitamin B_1, Stiebeling and Phipard state (p. 61):

> The average vitamin B_1 content of the diets of these families shows a gradual increase with rising weekly expenditures for food. Expenditures of $0.63-$1.24 a person a week bought

11. Swanson, C. O.: Wheat and Flour Quality, Minneapolis, Burgess Publishing Company, 1937.
12. Sherman, H. C.: The Chemistry of Food and Nutrition, ed. 4, New York, Macmillan Company, 1932.
13. Williams, R. R., and Spies, T. D.: Vitamin B_1, New York, Macmillan Company, 1938.
14. Stiebeling, Hazel K., and Phipard, Esther F.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities, Circular 507, U. S. Dept. Agric., January 1939.

diets containing from 280 to 330 international units of vitamin B_1 a requirement unit a day, respectively, in the case of white and Negro families in Southern cities. Less than a tenth of the white families of these cities, but about one third of the Negro families, were spending these amounts for food. The average vitamin B_1 content of their diets was scarcely two thirds of the fairly liberal suggested allowance.

The general reader may desire some comment on the meaning of the term "requirement unit." When dealing with families and other groups instead of individuals, it is obviously desirable both to take account of the requirements of the various individuals in the family and to deal with the family as a unit. The "requirement unit" represents an attempt to deal with this situation. Thus, Stiebeling and Phipard defined their unit as the need of an adult 20 years and over in age, and this requirement was set at 500 international units of B_1 or 1.5 mg. of pure thiamin, and given a value of 1.0 on a requirement scale. For boys 16 to 19 years of age the corresponding figures taken are 600 international units and 1.8 mg., respectively, or a factor of 1.2 on the "requirement scale." For children of other ages the respective figures range downward to those for children under 4 years of age, namely 200 international units, and 0.6 mg., and a factor on the requirement scale of only 0.4. A family consisting of both parents, a 16 year old boy and a 3 year old child would then require 2 plus 1.2 plus 0.4 or a total of 3.6 times the unit requirement, which would be equal to 1,800 units. This could also be expressed as 1,800 units divided by 3.6 requirement units to give "500 units a requirement unit." On this latter basis families can be compared, with the needs of the individual members also given their due consideration.

Another quotation much to the point is the following (p. 63):

> Of the entire number of white families participating in this survey, it is estimated that the 25 per cent choosing diets lowest in vitamin B_1 obtained less than 400 international units a requirement unit daily and 75 per cent, 600 or less international units a requirement unit a day. About 10 per cent selected foods furnishing less than 300 international units a requirement unit a day, and about half of the families obtained 500 or more international units of vitamin B_1 a requirement unit a day. . . .
>
> There is probably little danger of serious vitamin B_1 deficiencies if individuals *regularly select*[15] a goodly share of their needed calories from foods that have not been artificially refined or depleted of their vitamin B_1 by the processes of preparation. The relatively high vitamin B_1 value of diets of Southern Negro families, even when weekly food expenditures were low, was due to the fact that they consumed large quantities of whole corn meal, sweet potatoes and pork.

The words I have italicized should be emphasized in this connection because they really mean here that the factor of safety against vitamin B_1 shortage is not large: that these families in question must pay special attention to the matter of proper choice of foods if they are to obtain sufficient quantities of the vitamin. When particular attention must be paid to this matter, success will be determined in considerable measure by the knowledge of vitamin B_1 distribution in foods and the like which the families possess. Although we may pride ourselves on the high literacy rate characteristic of the American people by and large, we cannot but feel most dissatisfied with respect to the possession of detailed knowledge of food values on the part of the great mass of our population.

15. Italics are mine.

Jolliffe[4] has evaluated these Stiebeling-Phipard dietaries for vitamin B_1 content in two ways and estimated their respective factors of safety against vitamin deficiency. Using my vitamin/calory ratio as the criterion, the average of his calculations of the factor of safety afforded by these particular dietaries proves to be 14.4 per cent, with three of the eighteen groups yielding negative instead of positive values. When the Williams-Spies[13] thiamin/non-fat calories ratio is used as the basis of judgment, the average proves to be 18.3 per cent, with one group giving a negative value. It is unnecessary to discuss here the relative merits of the two modes of calculation employed, especially when they yield results so nearly the same. Let it suffice to call attention to the fact that these averages are not much above the average variations encountered in numerous biologic phenomena, such as, for example, basal metabolic rate. If, then, these American dietaries, the best averaged in with the poorer ones, afford a factor of safety against vitamin B_1 deficiency only moderately above what is estimated to be the requirement of normal healthy people, and the effects of diarrhea[16] and other fairly common conditions in increasing the amount of vitamin needed are also taken into account, one cannot fail to be impressed with the importance of considering measures for increasing the vitamin B_1 content of American foods. Additional evidence may be reported in support of the idea that many of our American dietaries are not optimal in content of vitamin B_1. Thus, Morgan and Barry[17] were able to show that the addition of B_1 rich materials to the diet of school children was associated with a definite increase in the growth rate; Summerfeldt,[18] and Ross and Summerfeldt[19] have also reported that the addition of vitamin B_1 containing materials to presumably adequate dietaries for children resulted in more rapid growth and improved nutritional status.

In all probability the present shortcomings of American dietaries with respect to vitamin B_1 content have not developed suddenly but are the result of a gradual change proceeding over a period of years. The food statistics that have been reviewed indicate that the per capita consumption of sugar has grown steadily for a century and has remained fairly uniform at a high level for only a few years. Such an increase has undoubtedly operated gradually to diminish the vitamin B_1 of our dietaries. The effect of the developments in wheat milling has been most pronounced since about 1870, with the highly refined wheat flour steadily gaining in use and popularity. I have not been able as yet to secure suitable American data on which to base calculations expressing more precisely this downward trend in B_1 content of dietaries in the United States. However, the conditions in this country have probably been fairly similar to those in England, particularly as affected by the growth of the sugar industry and the changes in the milling of cereals, the two dominant factors under consideration. Baker, Wright and Drummond[19] have made estimations of the probable B_1 content of various English diets used as far back as 1615. Table 2 is taken from their paper.

16. Dann, Margaret, and Cowgill, G. R.: Influence of Diarrhea on the Vitamin B_1 Requirement, Arch. Int. Med. **62**: 137-150 (July) 1938. Cowgill.[5]

17. Morgan, Agnes F., and Barry, Margaret M.: Underweight Children: Increased Growth Secured Through the Use of Wheat Germ, Am. J. Dis. Child. **39**: 935-947 (May) 1930.

18. Summerfeldt, Pearl: The Value of An Increased Supply of Vitamin B_1 and Iron in the Diet of Children, Am. J. Dis. Child. **43**: 284-290 (Feb.) 1932.

19. Ross, J. R., and Summerfeldt, Pearl: Value of An Increased Supply of Vitamin B_1 and Iron in the Diet of Children: II, Am. J. Dis. Child. **49**: 1185-1188 (May) 1935.

It will be noticed that about a hundred years ago (1838) there was some variation with respect to dietaries used in feeding the poor. The Poor Law applicable to the city of London provided a better diet as regards vitamin B_1 than that in force in Dudley Union. The most striking fact of interest in this connection is the observation that the paupers fed under the Poor Law of London in 1838 received approximately twice as much vitamin B_1 as the two highest income groups of London studied in 1937. It is difficult to escape the conclusion that the trend of vitamin B_1 supply over the past century has been definitely downward. If this condition is not now recognized and then made the basis of appropriate action, we may confidently expect to see our population as a whole in the same category as the masses of the Far East, where polished rice is the favored staple used in too great amounts with the consequence of a high average incidence of manifest beriberi. As was pointed out earlier in this paper, many clinicians have already convinced themselves that a dangerous situation in this respect has been reached.

PRACTICAL MEASURES

If the thesis is accepted that current American dietaries are not satisfactory in content of vitamin B_1, the question arises as to what practical measures might

TABLE 2.—*Probable B_1 Content of Various English Diets*

Date	Diet	Vitamin B_1 Yielded per Day, I. U.
1615	Suggested diet for seamen	640
1670	Soldiers' ration	1,000
1686	Patients in Barts	300-700
1782	Parish poor	650-850
1800	Diet of John Dalton	1,220
1836	Prisoners, Ipswich prison	700
1838	Poor Law, city of London	1,060
1838	Poor Law, Dudley Union	600
1937	London dietaries: two highest income groups*	450-550

* Cited by Baker, Wright and Drummond [18] as "Lloyd's data."

be taken to improve them in this respect. It seems unquestioned that we should continue to employ the educational process in every possible way in an effort to disseminate knowledge of food values in the widest possible manner. However, it has already been pointed out that emphasis on greater use of the "protective foods" cannot solve the problem of increased B_1 supply. In this connection the emphasis will have to be placed on greater use of legumes and nuts, but this line of action can be effective only within rather narrow limits because of the high energy value of these foods.

As a free people must necessarily exercise choices when securing their foods, one basic objective of all efforts directed toward improvement of our dietaries should be to see that, with the various foods readily available, it is exceedingly difficult for any one over a reasonable period, whether he knows a great deal about the science of nutrition or not, to make a set of food selections that is seriously in error. Putting the matter the other way, we should aim at making the conditions of food supply such as to yield with the greatest of ease diets that are excellent in every respect.

What lines of action are possible when attempting to deal constructively with this problem? In the educational work emphasis could be laid on greater use of the "undermilled" cereal products, under which heading shall be included whole-meal flour and other fractions, such as middlings. In view of the experience of governmental and health authorities in the Far East dealing with the problem of too great use of polished rice to the exclusion of the undermilled varieties, this plan of attack would probably be of only limited usefulness. No doubt a certain small fraction of the population will respond to educational efforts emphasizing the high B_1 value of the undermilled cereals, and to this extent such efforts will yield satisfactory returns. The greater part of the population will still find the white highly milled flour possessing the greatest appeal, if past experience is any indication. The development of modern transportation facilities, the necessity of marketing cereals in forms that are stable for long periods and other factors peculiar to our modern complex civilization will, in my opinion, continue to give to white flour a position of prominence in our dietaries sufficiently great to mean essentially a continuance of our basic problem.

The isolation and availability through chemical synthesis of pure vitamin B_1 offers another line of attack. It is possible to add the vitamin to wheat flour in any desired and appropriate amount. Whether this is economically feasible at the present time, I leave to others to decide. No doubt also there are certain technical industrial questions involved here, but it is reasonable to believe that these are amenable to solution by research directed specifically toward that end.

In suggesting that vitamin B_1 be added to cereals, particularly wheat flour, it is pertinent to point out that flour functions essentially as a basic staple food entering into the baking of numerous special products. It is used in the manufacture not only of bread but of cakes, crackers, cookies and the like. There are, of course, many kinds of wheat flour, some suitable for making bread, others more useful for cakes, crackers, cookies and the like. For the purposes of the present discussion the word "flour" may be understood to mean all these highly milled products of the wheat berry regarded as a basic staple class of products. If this basic staple could be made a carrier of vitamin B_1, the entire pastry group of foods would no longer stand out in any dietary as essentially devoid of vitamin B_1, as is now the case. It seems reasonable to believe that through the one act of adding the vitamin to the wheat flours as a group we would increase directly the vitamin B_1 intake of a greater part of our population than could be affected by any other single step. The alternative is to encourage each of the many units of the entire baking industry to add the vitamin to its particular products. It is probably too much to expect any large measure of success in such a campaign.

How much vitamin B_1 should be added to wheat flour and other foods worthy of consideration in this connection? One cannot, of course, be dogmatic in answering this question. However, the following ideas are believed to be worthy of consideration:

Vitamin B_1 is now believed to play a role in energy metabolism, probably in the metabolic transformation of carbohydrate in the body.[20] It seems logical, therefore, to consider that any addition of it to a food should be made in some relation to the energy value of that food. This gives a principle applicable to a variety of foods. Another principle applicable to a refined product, wheat flour, for example, is that the vitamin be added in amounts sufficient to make its concentration approximate that present in the original unprocessed food; in the case of wheat flour this would mean adding enough vitamin B_1 to make the flour approximately equal in vitamin content to the original wheat kernel. This might be called the principle of "restoration" to be distinguished from that of "fortification," by which

20. Cowgill,[3] Williams and Spies.[19]

is meant the addition of vitamin in such amounts as to make the concentration even greater than that of the original natural product or what the most liberal estimate of the human need for substance would indicate to be desirable.

In this connection the problem of addition of vitamin B_1 to purely artificial food mixtures designed to be more or less perfect in a nutritive sense is worthy of mention. It seems obvious that the principle of restoration can hardly apply to such situations, whereas that of securing a desirable value for the vitamin/calory or thiamin/carbohydrate-calory ratio in the final product seems peculiarly appropriate.

Elsewhere [6] it has been pointed out that the need of adults seems to be not less than about 10 international units of the vitamin per hundred calories; children apparently require amounts ranging from 20 to 25 international units per hundred calories. The wisdom of adding the vitamin to foods in such amounts as to give at least 25 international units per hundred calories would seem to be unquestioned, because this would be bringing the product up to the irreducible minimum for a child and making it a little better than that needed by an adult. The desirability of a higher standard than this is therefore obvious. If the "restoration" of wheat flour and related grain products is taken as our guiding principle, flour would contain approximately twice the minimum for children that has been mentioned. Another point of view, valuable in this connection, relates the amount of vitamin in the "restored" product to the quantity obtained daily when customary amounts of the product are eaten. The effect of a substitution in present dietaries of "restored" flours should be essentially a "restoration" of our present dietaries to those in common use a century ago and discussed earlier in this paper. In quantitative terms this would mean that our average daily diet would contain from about 1,000 to 1,200 international units of the vitamin instead of the present 450 to 550 units.

The question might well be asked: Should wheat flour and related foods ever be given more vitamin B_1 than sufficient to "restore" them to the native cereal from which they were obtained, and if so, what limitation to such "fortification" would be reasonable? In attempting to answer this question one might draw on the scientific literature dealing with the problem of relative requirements for special situations, lactation for example, in contrast to that for mere maintenance of the adult or for normal growth of the young. Studies of lactation in the rat [6] indicate that, in order to nurse a litter successfully to weaning, the mother rat requires from three to five times as much vitamin B_1 as she requires for her own maintenance metabolism. Mention has already been made of studies indicating that growing children show optimal retention of B_1 when receiving about 25 international units per hundred calories. This may be compared with an estimate of about 10 international units per hundred calories needed by the adult. Here the factor proves to be 2½. Evidently a factor of safety of at least 3 could be regarded as having some scientific justification. From this point of view one is led to the suggestion that the addition to a food product intended for general use of thiamin in such amount as to give 75 international units per hundred calories could be regarded as reasonable, although this concentration would in fact exceed somewhat that characteristic of the whole grains. Perhaps the simplest solution of the question would be to take the highest natural concentration in the class of whole-grain foods as the standard of maximum to apply when the vitamin is being added to a *general purpose* food. Greater concentrations, representing true "fortifications," could then characterize *special purpose* foods, and in such cases the amount of vitamin to be added could be determined by the particular purpose aimed at in the preparation of the product, and other pertinent considerations.

This principle of securing a desirable vitamin/calory ratio is, after all, not anything really new. Students of nutrition have long related the minimal needs for other factors to the energy yielded by the diet. For example, the requirement of calcium is often stated as being not less than 23 mg. per hundred calories, that for phosphorus at least 44 mg. per hundred calories, that of iron about 0.5 mg. per hundred calories and so on.

As living organisms tend to regulate their food intake to meet their energy needs, probably because the requirement for this factor is so dominant in most situations, it is logical to relate the demands of non-energy yielding nutrients to the caloric need. What may be new in the suggestion made here is the application of this principle to individual foods instead of the dietary as a whole or the person consuming the food. Such a use of this principle appears warranted, particularly when foods are to be manipulated, so to speak, to be modified by addition of special desirable factors, and this is essentially the situation presented by the problem under consideration. The application of this principle, particularly with respect to vitamin B_1, to wheat and other grains and their products now constituting such a large part of the American dietaries would, in my opinion, be definitely in the interest of public health and welfare.

Students of the vitamins are aware that these important dietary factors are now exploited vigorously in the pharmaceutic trade. It is my opinion that the American people should, if possible, obtain their needed vitamins from foods rather than from pharmaceutic preparations. The preparations available in the local drug store should be those desired by the physician in the treatment of special cases which involve vitamin deficiencies. It is certainly not the ideal solution of our basic problem of improving the general nutrition of the American people to advocate that they make greater use of the various vitamin B_1 preparations now available essentially as pharmaceuticals, because the people most in need of the vitamin happen to be those with the least money to spend for necessities. We are thus brought around to the need for improving our important widely available and widely accepted foods. If certain basic energy-rich staples are made the appropriate carriers of the needed vitamins, as was pointed out previously, this single step affects more persons in the desired way than any other that can be devised.

SUMMARY

There are grounds for believing that American dietaries as a whole are unsatisfactory with respect to the content of vitamin B_1. The examination of available food statistics as well as of recently collected American dietaries, the observations of clinicians concerning the high therapeutic value of vitamin B_1 in conditions hitherto not suspected to be due to lack of this factor, and the observations of the value of added vitamin B_1 to the dietaries of many children all support this belief. It is believed that prosecution of a program fostering addition of vitamin B_1 to staple American foods according to the principles discussed in the present report would be definitely in the interests of the public.

113
939

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street - - - Chicago, Ill.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - Eight dollars per annum in advance

Please send us promptly notice of change of address, giving both old and new; always state whether the change is temporary or permanent. Such notice should mention all journals received from this office. Important information regarding contributions will be found on second advertising page following reading matter.

SATURDAY, DECEMBER 9, 1939

The Platform of the American Medical Association

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

SPONTANEOUS PANCREATIC HYPOGLYCEMIA

In The Journal, ten years ago, appeared a report by Howland, Campbell, Maltby and Robinson,[1] of Toronto, describing a case of dysinsulinism of six years' duration in which there were attacks of coma and convulsions. These attacks were found to be caused by low blood sugar levels and could be warded off by the administration of food. The case was diagnosed as an islet cell tumor of the pancreas; Roscoe R. Graham found and removed a tumor which the authors considered to be a slow growing carcinoma of the islands of Langerhans and from which insulin could be recovered. The patient made a complete recovery. A more recent report by Campbell, Graham and Robinson,[2] of the same clinic, states that the patient has now been well and free from any disability related to the uncontrolled overproduction of insulin for more than ten years.

The protean manifestations of the hypoglycemia complex have been exhaustively treated by Harris, Whipple, Wauchope and Sigwald. However, unless one becomes, as Harris puts it, "hyperinsulinism conscious," diagnostic errors may yield diagnoses ranging all the way from neurasthenia to epilepsy and brain tumor.

Banting and his associates recognized the dangers which may arise from reducing the blood sugar too far below the normal level. The most commonly observed manifestations of insulin shock are nervousness, trembling, weakness, faintness, hunger which may be agonizing, vertigo, diplopia, mental confusion resembling alcoholic intoxication, excitement, amnesia, dysarthria, sensory and motor aphasia, delirium, coma and convulsions. Harris[3] in 1924 conceived of hyperinsulinism or dysinsulinism as a clinical entity and described cases of low blood sugar in which the symptoms were improved by feeding. Hyperinsulinism or hypoglycemia appeared to be the antithesis of hypo-insulinism of diabetes.

In 1927 Wilder[4] and his associates reported a case of hypoglycemia requiring, at the time of observation, as much as 25 Gm. of dextrose an hour to prevent convulsions. Exploratory operation by William J. Mayo revealed a large nodular pancreas with metastases to the liver. In microscopic studies the cells of this cancer bore a striking resemblance to the cells of the islands of Langerhans. Alcoholic extracts made from the cancer tissue in the liver acted like insulin on injection into rabbits. This was the first conclusive evidence of hyperinsulinism due to tumor of the islands of Langerhans.

1. Howland, Goldwin; Campbell, W. R.; Maltby, E. J., and Robinson, W. L.: Dysinsulinism: Convulsions and Coma Due to Islet Cell Tumor of the Pancreas, with Operation and Cure, J. A. M. A. **93**: 674 (Aug. 31) 1929.

2. Campbell, W. R.; Graham, R. R., and Robinson, W. L.: Islet Cell Tumors of the Pancreas, Am. J. M. Sc. **198**: 445 (Oct.) 1939.

3. Harris, Seale: The Diagnosis and Treatment of Hyperinsulinism, Ann. Int. Med. **10**: 514 (Oct.) 1936.

4. Wilder, R. M.; Allan, F. N.; Power, M. H., and Robertson, H. E.: Carcinoma of the Islands of the Pancreas: Hyperinsulinism and Hypoglycemia, J. A. M. A. **89**: 348 (July 30) 1927.

In the next decade the number of cases diagnosed and successfully treated or identified at necropsy increased to about 100; the largest single series were those of Whipple and of Womack and Leary. The cases fall into two groups: (1) those with morphologic changes in the islands of pancreas and (2) those without detectable alterations in the pancreas. The organic changes are of three types: (1) general hypertrophy and hyperplasia of the islands of Langerhans, (2) adenoma and (3) carcinoma. Carcinoma of the islands appears to be rare, not more than thirteen cases being reported in the literature. Islet adenomas, on the other hand, are common and deserve special mention. Frantz and Whipple [5] compiled twenty-one cases of islet adenomas found at operation and ten at necropsy, to which Womack added fourteen. These unusually small tumors are situated most frequently in the tail and less frequently in the body or the head of the pancreas. The tumors are reddish and are clearly demarcated from the normal pancreatic tissue. They are usually single but may be multiple. Microscopically they consist of beta cells of varying degrees of maturity. While the concentration of insulin in these tumors was found to be from four to forty times that of normal pancreas, the total amount was not equal to that of normal pancreas. The hyperinsulinism or dysinsulinism is probably due to the fact that the production and release of insulin from the islet cells of the adenoma is not under the neurohormonal control which so delicately balances this process in a normal pancreas.

The diagnosis of pancreatic hypoglycemia is made from a careful consideration of the anamnesis and repeated determinations of fasting blood sugar and dextrose tolerance. Sooner or later the patients notice the association between attacks and hunger. The eating of sweet food is most effective in relieving the symptoms. In the differential diagnosis, hypoglycemia due to disturbances of the liver, the hypophysis or the adrenal glands must be eliminated. Dietetic treatment may prove successful in the milder cases and may be tried. Progression of the symptoms, however, justifies surgical intervention. The best results thus far have been obtained in cases of islet adenomas. Womack [6] states that "clinical surgery offers few examples where the recovery is so complete or so dramatic as from the complete removal of an islet tumor." Resection of the greater portion of the pancreas in cases without pathologic changes has not been as successful. Among the notable exceptions is the remarkable case reported by Graham and Hartmann [7] in which from 80 to 90 per cent of the pancreas was removed from a baby 1 year of age for chronic hypoglycemia with repeated convulsions and marked retardation in mental development. All the symptoms promptly disappeared and have not recurred. The mental and physical states of the patient have shown marked improvement since the operation. The pancreatic tissue removed was essentially normal.

5. Whipple, A. O., and Frantz, Virginia K.: Adenoma of the Islet Cells with Hyperinsulinism, Ann. Surg. **101**: 1299 (June) 1935.
6. Womack, N. A.: Hypoglycemia Due to Adenoma of the Islets of Langerhans, South. M. J. **27**: 135 (Feb.) 1934.
7. Graham, E. A., and Hartmann, A. F.: Subtotal Resection of the Pancreas for Hypoglycemia, Surg., Gynec. & Obst. **59**: 474 (Sept.) 1934.

INDUSTRIAL UTILIZATION OF DAIRY PRODUCTS

Of the hundred billion pounds of milk produced annually in the United States, 46 per cent is separated to obtain cream. The skim milk which results from this operation contains vast amounts of substances which are of industrial importance and for which new uses are being sought. Skim milk, for instance, is rich in casein and lactose. Similarly, a high percentage of lactose is present in the whey obtained in the manufacture of cheese. Particularly during the last few years a considerable amount of attention has been centered on the industrial utilization of some of the by-products of the dairy industry, and a number of the achievements which have been made in this direction were discussed at a recent symposium.[1]

Casein has long been used in the manufacture of various types of adhesives and may also be used to prepare plastic materials such as artificial horn or artificial ivory. A few years ago a process was discovered for converting casein into textile fiber and this new use is now attracting attention in several countries. At present Italian, Netherland and British firms are reported to be engaged in producing casein fiber, and a patent for its production has already been granted in the United States. The European production of casein fiber in 1938 was probably between six and eight million pounds. The high cost of silk induced the development of rayon and, in the same sense, the comparatively high cost of wool has given impetus to a search for cheaper substitutes. In this country there is reportedly a potential annual supply of skim milk of forty billion pounds over and above that now converted into industrial products and, according to investigators in the United States Department of Agriculture,[1] it should be possible for casein fiber to be produced much more cheaply than wool. Whether or not casein fiber will be used extensively in this country as a diluent or extender of wool remains to be seen. Stable kinked rayon is being used for this purpose at present, but casein fiber has the important advantages that it can be dyed with wool dyes and can be laundered by the same methods as wool.

Whey is obtained in large quantities as a by-product both in the manufacture of cheese from whole milk and in the manufacture of casein from skim milk. As improved transportation facilities permit the bringing of more milk to centrally located factories, not only is the farmer deprived of a valuable feed but the disposal

1. Whittier, E. O., and Gould, S. P.: Indust. & Engin. Chem., News Edition **17**: 369, 1939. Smith, L. T., and Claborn, H. V., ibid. **17**: 370, 1939. Papers presented as part of the Joint Symposium on the Industrial Utilization of Dairy Products before the Divisions of Agricultural and Food Chemistry and Biological Chemistry at the ninety-seventh meeting of the American Chemical Society, Baltimore, April 4, 1939.

of whey becomes a problem. Cheese factories converted more than a million pounds of whey into powder in 1937, and investigators in the United States Department of Agriculture have already devised a process for separating the whey powder into lactose, a protein-rich concentrate, and a solution rich in vitamin G. The lactose may be used in medicinal preparations and in infant foods as well as in the manufacture of candy. The production of lactic acid by fermentation of the lactose in whey is also a commercial activity at the present time, and the lactic acid thus produced has a wide variety of uses as an acidulant in food products such as fruit essences, extracts, syrups and baking powder. It has even been used recently in effervescent beverages in the place of citric acid. Certain esters of lactic acid may also be converted by suitable treatment into methyl acrylate, for which there is a wide variety of possible uses in the manufacture of plastic materials. It seems probable that in the near future lactic acid will play an increasingly important part in the field of solvents, in plastics, and as an acidulant for beverages and foods.

Important advances have been made in the direction of the utilization of by-products of the dairy industry. These developments are of particular interest as they involve the important nutrient milk. Moreover, some of the by-products may, in turn, be incorporated in certain foods as well as used in the manufacture of pharmaceuticals.

Current Comment

HISTAMINE IN PLATELETS OF RABBITS

From experiments originally intended to demonstrate the changes in blood histamine following vaccine administration, Zon, Ceder and Crigler [1] obtained evidence suggesting that it is the platelets which carry major portions of the blood histamine. The rabbits in the experiment were sensitized to a strain of beta-hemolytic streptococcus of low virulence. Following the intravenous administration of 10 cc. of the killed homologous vaccine to sensitized animals and also to nonsensitized controls, blood samples were withdrawn and platelets, white cells and histamine were determined. There was an almost complete disappearance of granulocytic cells following the vaccine with little change in the total histamine content. Further, there was no increase in plasma histamine, which ruled out any shift in histamine from injured white cells to plasma. It was also shown that the administration of antiplatelet serum caused a significant drop in blood histamine generally paralleling the drop in platelets. Likewise fractional centrifugation of platelet containing plasma removed histamine almost in the same proportion as the platelets. This demonstration of the distribution of histamine should be of importance in future investigations on this interesting blood constituent.

1. Zon, Leo; Ceder, E. T., and Crigler, Catherine W.: The Presence of Histamine in the Platelets of the Rabbit, Pub. Health Rep. 54:1978 (Nov. 3) 1939.

"TIME" MARCHES ON!

In the issue of *Time* for December 4 appeared an article entitled "Misery Harbor," purporting to describe the recent changes in the administration of the Cook County Hospital in Chicago. The title "Misery Harbor" is taken from a series of articles which appeared in the Chicago *Daily Times* following an investigation of the hospital made by that newspaper more than a year ago. The article in *Time* is mentioned here because it is replete with absolute misstatements of fact beyond anything of a similar character published in the field of medicine even in that periodical during recent years. Indeed the article betrays a carelessness almost incomprehensible in a periodical which has in the past frequently gone to extended lengths to secure accuracy.

Briefly there follows a list of statements made by *Time* and thereafter the correct statement:

1. "During the last four years Cook County Hospital has been a battleground for two warring medical factions." There has been no battle between two warring medical factions.

2. "Last week a compromise ended the fight." There has been no compromise.

3. "Dr. Meyer never required the hospital's army of interns to attend postgraduate classes or lectures." Lectures and conferences for interns have been held for at least ten years.

4. "The American Medical Association . . . believes that all interns should taper off into actual practice with at least eighty hours of medical lectures during internship." No specific number of hours of instruction has ever been mentioned, much less required, by the Council on Medical Education and Hospitals.

5. "*Consequently*, four years ago, the A. M. A. dropped Cook County Hospital from its list of approved hospitals . . ." Obviously the number of lecture hours was in no wise involved.

6. "Over this point Cook County's Dr. Meyer and A. M. A.'s education secretary, Dr. Irving Samuel Cutter . . ." Dr. Irving S. Cutter is not the A. M. A.'s education secretary; he is Dean of Northwestern University School of Medicine.

7. ". . . thus automatically cutting off Dr. Meyer's supply of interns from topflight medical schools." At no time has the County Hospital failed to obtain interns from the four recognized medical schools of Chicago. No others are eligible for appointment.

8. ". . . A. M. A. last spring brought public opinion to bear." At no time has the A. M. A. made any attempt to influence public opinion concerning the County Hospital. It has studiously refrained from comment upon the situation.

9. "An A. M. A.-inspired citizens' committee . . ." The A. M. A. had nothing whatever to do with the "Citizens' Committee" which was appointed by the Board of County Commissioners upon the recommendation of a committee of hospital experts previously employed by the County Board to investigate and report upon conditions at the County Hospital.

10. Said committee ". . . hinted that the hospital might be reinstated on the A. M. A.'s list if a new director acceptable to the A. M. A. were chosen." As stated above, the Citizens' Committee had no connection whatever with the A. M. A. and therefore could not and did not claim to represent it.

11. "2) Cook County was promised reinstatement on the A. M. A.'s list some time around Jan. 1; . . ." No such promise was given.

Immediately on the appearance of this article a telegram was sent to *Time* calling attention to some of these inaccuracies. The inaccuracies are all the more unfortunate because it would have been exceedingly simple merely by the use of the telephone, since *Time* is printed in Chicago, to secure the facts. It will be interesting to see how far *Time* goes in its correction.

ORGANIZATION SECTION

THE SIXTEENTH DECENNIAL CENSUS IN 1940

PREPARED ESPECIALLY FOR THE JOURNAL BY THE BUREAU OF THE CENSUS

There is one division of the Bureau of the Census with which every doctor in America who has ever lost a patient or attended at the birth of a new one has had contact, whether he knows it or not, and that is the Division of Vital Statistics. Eventually, through one means or another—state bureaus of public health, usually—every birth and death certificate issued in America reaches the office of the division, where, along with the millions of others of its kind, it is added to the records from which our national birth and death rates are computed, the incidence of death from certain major diseases, which the division calls "The Killers," is ascertained, the frequency of death by accident, and what type of accident, is figured and a dozen or so other enormously valuable sets of vital statistics are acquired, on the basis of which state boards, county organizations, hospitals, medical associations and individual doctors themselves can plan medical campaigns, campaigns for public health and safety, and budgets for sanitary and institutional improvements.

But the great ten year census of population, the sixteenth such, to begin April 1, 1940, will add a large amount of invaluable data to the files of the medical profession. And along with it, the biennial census of manufactures and a similar one of business, both of which begin January 2 of the coming year, include statistics of a different type which are also of real value to the doctor.

Perhaps the most interesting one of the specific questions being asked in the census schedules next year is that which is being put to the druggists of this country on the questionnaire of the business census. Druggists and pharmacists are being asked what the dollar volume of their sales was in the form of doctors' prescriptions. That figure, alongside the one giving the total sales of "drugs, medicines, chemicals, compounds," will give the physician an accurate picture of the comparative amount of money being spent for proprietaries and for prescriptive medicines. These data will be broken down into state figures and when possible into figures for large cities. A further question to be asked, of some interest to the medical profession, is on the number of registered pharmacists employed. The need for skilled chemists in the average drug store is known to all physicians, and figures on the pharmacists' profession may have a tendency to increase the quality and quantity of trained personnel in this field.

The Census of Business will tabulate all drug stores by states, counties and cities and towns of 2,500 population or more. They will be listed in two main groups—those with soda fountains and those without. Each will be asked to report on the sales of various kinds of commodities sold and to give inventory totals for the beginning and close of 1939.

The Census of Manufactures, which will be taken concurrently with the business census, will present important national, state and city totals on the production of drug grinding, drugs and pharmaceuticals, biologicals and proprietary medicines. Data on this type of manufacture will be presented only by states, but important totals on the production of major specific commodities in the drug industry will be presented in such a fashion that the medical profession will be able to draw material conclusions on trends in medication in this country. Included here also will be a breakdown between prescriptive and proprietary drugs and medicines.

The Census of Manufactures will also present valuable tables on the production of surgical appliances, rubber goods and other accessories of the doctor and will thus give something of an index of the state of health of the medical and surgical professions as a whole, and changes and trends in the use of various standard appliances and materials.

But the most important of all the censuses to be taken in 1940, for the country as a whole as well as for the physician, will be the sixteenth Decennial Census of Population. This will be the one hundred and fiftieth anniversary of the first population census in America, and, partially in celebration of the event, an effort has been made to have the census schedules more comprehensive, more scientific and more generally useful to every type of person or profession interested in people than ever before. The census itself is a task large enough to stagger the imagination. More than 130,000 enumerators will be employed for a period averaging one month—the month of April—and will be trained in the technics of census taking by 560 district supervisors. To synchronize and supervise operations as a whole, 105 area supervisors will be located in as many key cities to serve as courts of appeal and general managers of the whole enormous project.

Vitally important will be the social, economic and scientific results of the tabulations of specific answers to the various questions on the population census schedules; and it is here that the interests of the medical profession are closely involved. There are two major ways in which the population census is of importance to all physicians:

The first concerns the profession itself. The 1940 census will show, with a high degree of accuracy, exactly what the distribution of doctors is throughout the country. The figures will be presented by states, by cities of 100,000 and over and by cities of from 25,000 to 100,000 and will give the exact numbers of physicians and surgeons, osteopaths, nurses, veterinary surgeons and dentists, as well as such "semiprofessional" classifications as chiropractors, "healers, not elsewhere classified," technicians and laboratory assistants, and physicians', surgeons' and dentists' assistants. By a careful study of these data individual practitioners, state and county medical associations, hospitals and state and municipal public health groups can arrive at sound conclusions concerning the number of doctors in particular areas and the need for more such professional men, if any. The serious problem of the unequal distribution of medical men throughout the country can thus be scientifically approached by means of the census data.

Figures of this sort can obviously be of enormous value not only to the groups that have been named but

to the country's legislative bodies in their attempt to establish higher types of requirements for medical practice and to supply their areas with more ample institutional quarters.

The other part of the population census of especial interest to the medical profession is the general data on distribution of population itself, with especial emphasis on sex and age differentiations. These compilations draw into the picture problems of a broader social interest than those dealing specifically with the profession. The 1940 census will present accurate figures, for instance, on the extent of the decline in the birth rate in the United States and the consequent increase in the number of aged persons. Resulting from this may be many changes of decision on the part of young students in medical schools who might have decided to take up obstetrics or allied branches of medicine or surgery but who will feel that the decline in the birth rate may have catastrophic results on their practice as the trend increases and the number of babies born drops. Hospitals and sanatoriums may find such figures of value in case they plan any expansion, for, as the birth rate declines, the rate and number of aged persons increases, and the need for old age homes and for hospitals devoted to the care of diseases of the aged increases over and above the need for lying-in hospitals.

This whole problem of a declining birth rate is, of course, one of national importance, which has reverberations far beyond the medical profession alone. Similarly the question of the trends in population shift are countrywide in significance, in addition to having a very definite bearing on the question of distribution of medical services. There seems recently to have come a stop to the tendency of people to move to the cities from the farm, but it is impossible to tell, without the data from the 1940 census, how large or how significant this change of trend is.

There are naturally many specific problems in the medical profession on which the census cannot touch, such as professional standards and scientific advances in surgical technics and the materia medica. Material of this sort is the specific province of the American Medical Association, and its data are more complete, more accurate and more up to date than any similar figures could be when taken on a broad population basis. But it remains that the largest problems confronting the profession are those which are dealt with by the Bureau of the Census in its forthcoming decennial census and in the Division of Vital Statistics in its frequent releases on causes of death, hospital statistics, birth registration and so on.

Certainly if there is one government department of supreme value to physicians as a whole, it is the Bureau of the Census. If all members of the profession will remember this when the census enumerators call on them sometime in April and cooperate to the best of their ability in the filling out of the schedules promptly and accurately, they can be assured that the resultant data will be just that much more valuable to them, once they are compiled and published. And if any of the questions seem to the individual physician to be somewhat personal and private in nature, he should remember that all information collected by the enumerators is held strictly confidential by them and by the statisticians and population scientists in Washington; that they are under oath never to reveal any of the information which goes through their hands either to individuals or to any society, association or government department whatsoever; and that Congress has made the answering of these questions obligatory on the individual, in an effort to assure the country as a whole of accurate, complete and therefore socially valuable statistics concerning the people of America.

With the cooperation of the medical profession freely and willingly granted to the census enumerators, doctors can be assured that the results of the 1940 decennial census will be of such a nature as to aid them greatly in their personal affairs, their local and state problems, and the national problems of health as a whole.

WOMAN'S AUXILIARY

Colorado

The annual meeting of the auxiliary to the Colorado State Medical Society was held in Colorado Springs October 5-7. Dr. H. E. Harms was speaker at the luncheon meeting, which was attended by 120 auxiliary members and guests.——More than eighty members attended the first autumn meeting of the auxiliary to the Denver County Medical Society, which was held at the Denver General Hospital October 18.

Florida

The Palm Beach Medical Society and the auxiliary entertained doctors and their wives who attended the third annual meeting of the Southeast District Medical Society in West Palm Beach October 12. An auxiliary to the district medical society was organized, and Mrs. H. A. Leavitt, Miami, was elected president. Speakers at the meeting were Mrs. L. C. Ingram, president of the auxiliary to the Florida Medical Association; Mrs. Leigh Robinson, chairman of the *Hygeia* committee, and Mrs. J. W. McMurray, chairman of the exhibit committee.

Illinois

Mrs. Charles C. Winning, president of the auxiliary to the Illinois State Medical Society, spoke on auxiliary activities at a meeting of the auxiliary to the Vermilion County Medical Society in Danville October 3 and at a meeting of the auxiliary to the Logan County Medical Society in Lincoln October 26.

Group hospital insurance was discussed by Enoch J. Brand at a joint meeting of the Adams County Medical Society and its auxiliary in Quincy October 9. The auxiliary to the Knox County Medical Society met at the Galesburg Club, Galesburg, October 20. Articles from THE JOURNAL on the national health program were read, and plans were made for distributing *Hygeia* in the county.

The auxiliary to the Will-Grundy County Medical Society met in Joliet October 10. Reports were given on articles published in *Hygeia* and the *Illinois Health Messenger*. Members were asked to study editorials and sections devoted to medical economics in THE JOURNAL and the *Illinois Medical Journal*.

Mrs. W. J. Wanninger, chairman of the *Hygeia* committee of the auxiliary to the Illinois State Medical Society, addressed a group meeting of the auxiliary to the Chicago Medical Society at the home of Mrs. William D. Cutter October 16. Mrs. Wanninger emphasized the importance of placing *Hygeia* in the schools and reading rooms of every community in Illinois. Dr. Charles Papik discussed "An Old Age Plan for Doctors and Their Wives" at a group meeting of the auxiliary to the Chicago Medical Society at the Englewood Hospital.

Members of the Irving Park group of the auxiliary to the Chicago Medical Society met at the Municipal Tuberculosis Sanitarium, September 26. Addresses were given by Drs. Henry C. Sweany, Richard M. Davison and Meyer Lichtenstein, members of the staff of the Sanitarium.

Iowa

The board of directors of the auxiliary to the Iowa State Medical Society met in Des Moines September 22; Mrs. Edward A. Hanske, Bellevue, is president. Mental hygiene is the topic of study for the year. The Speakers' Bureau, the Hygeia clipping bureau and copies of radio broadcasts on health will be used by the Committee on Public Relations for its work during the year.

Louisiana

The auxiliary to the Caddo Parish Medical Society met in Shreveport October 11. Mrs. S. M. Blackshear, president of the auxiliary to the Louisiana State Medical Society, spoke on the aims and accomplishments of the state auxiliary. Mrs. Blackshear was speaker also at the first quarterly meeting of the auxiliary to the Lafayette Parish Medical Society in Lafayette October 19. Mr. Gung-Hsing Wang, Chinese vice consul, spoke on "The International Situation Through the Chinese Window" before the auxiliary to the Orleans Parish Medical Society in New Orleans October 11. A committee was formed to do extra work for the Red Cross and to assist in raising funds for the Community Chest.

Dr. John Pracher, president, Ouachita Parish Medical Society, addressed the members of the parish auxiliary at a meeting in Monroe October 12 on the subject "Blood Transfusion." The auxiliary to the Second District Medical Society met in Norco October 17; Mrs. S. M. Blackshear addressed the members. ——The wife of every member of the St. Tammany Parish Medical Society is a member of the auxiliary.

Tennessee

The board of directors of the auxiliary to the Tennessee State Medical Association met in Nashville September 29. Following the business session and luncheon, Mrs. Matt B. Murfree, of Murfreesboro, president of the auxiliary, read "The Eulogy of the Doctor," written by Robert Louis Stevenson.

The annual social meeting of the Knox County Medical Society and its auxiliary was held September 16 at the home of Dr. and Mrs. J. B. Neil. About 100 physicians and their wives were in attendance.

Wisconsin

More than 125 members and guests attended a meeting of the auxiliary to the Milwaukee County Medical Society in Milwaukee October 13. Prof. Harold Ehrensperger of Northwestern University, Evanston, Ill., spoke on "Drama and Propaganda."

OFFICIAL NOTES

THE NEW YORK SESSION

Section Representatives to the Scientific Exhibit

The various sections of the Scientific Assembly have appointed representatives to the Scientific Exhibit to assist and advise in the procurement and selection of exhibits for the New York session, June 10-14, 1940. The following appointments have been made:

Practice of Medicine—Fred M. Smith, Iowa City.
Surgery, General and Abdominal—Grover C. Penberthy, Detroit.
Obstetrics and Gynecology—H. Close Hesseltine, Chicago.
Ophthalmology—Georgiana Dvorak Theobald, Oak Park, Ill.
Laryngology, Otology and Rhinology—Daniel S. Cunning, New York.
Pediatrics—Arthur F. Alt, Chicago.
Pharmacology and Therapeutics—Wallace M. Yater, Washington, D. C.
Pathology and Physiology—F. W. Konzelmann, Philadelphia.
Nervous and Mental Diseases—F. P. Moersch, Rochester, Minn.
Dermatology and Syphilology—Hamilton Montgomery, Rochester, Minn.
Preventive and Industrial Medicine and Public Health—Paul A. Davis, Akron, Ohio.
Urology—John H. Morrissey, New York.
Orthopedic Surgery—Mather Cleveland, New York.
Gastro-Enterology and Proctology—Sara M. Jordan, Boston.
Radiology—S. W. Donaldson, Ann Arbor, Mich.

Application blanks for space in the Scientific Exhibit may be obtained from the section representatives or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago, Ill.

RADIO BROADCASTS

The seventh season of broadcasting by the American Medical Association over the facilities of the National Broadcasting Company and affiliated stations is now under way with programs scheduled each Thursday at 4:30 p. m. eastern standard time (3:30 central standard time, 2:30 mountain time and 1:30 Pacific time). The program is on the Blue network of the National Broadcasting Company, the key station of which is WJZ, New York.

It is impossible to publish a list of topics in advance when programs are developed from last minute proof pages of THE JOURNAL. It is possible to say that future programs under consideration involve one each dealing with progress in medicine, rabies, infantile paralysis, maternal and child health, hospitals, medical education and industrial health. These programs will be as appropriate as possible to the season at which greatest interest in these topics is manifested. The programs on hospitals, medical education and industrial health will correspond with publication dates of special numbers of THE JOURNAL devoted to these topics. The program on medical progress will be broadcast December 28. The programs on maternal and child health will be a part of the spring series.

A special program in cooperation with the National Foundation for Infantile Paralysis, Inc., and the Committee for the Celebration of the President's Birthday is scheduled to appear as the regular program dated January 11.

Lists of radio stations which have signified their intention of broadcasting Medicine in the News, according to information received from the National Broadcasting Company, were published in THE JOURNAL, December 2, page 2065.

EDUCATION AND LICENSURE

The thirty-sixth Annual Congress of the Council on Medical Education and Hospitals of the American Medical Association will be held at the Palmer House, Chicago, Feb. 12 and 13, 1940. The Federation of State Medical Boards of the United States will participate in the congress. Topics and speakers are as follows:

Report of the Council on Medical Education and Hospitals.
Ray Lyman Wilbur, M.D., LL.D., Chairman, Stanford University, Calif.

(Subject to Be Announced.)
Alan Gregg, M.D., Director, The Medical Sciences, Rockefeller Foundation, New York.

Professional Education.
C. S. Boucher, Ph.D., Chancellor, University of Nebraska, Lincoln.

The Goal of Medical Education.
Irvin Abell, M.D., Vice Chairman, Board of Regents, American College of Surgeons, Louisville, Ky.

Graduate Work in Medical Areas.
George D. Stoddard, Ph.D., Dean, Graduate College, State University of Iowa, Iowa City.

Trends in Liberal Arts Education.
George A. Works, Ed.D., Professor of Higher Education, Department of Education, University of Chicago.

The Place of Malignant Disease in the Medical Curriculum.
Ludvig Hektoen, M.D., LL.D., Executive Director, National Advisory Cancer Council, Washington, D. C.

Medical Education—1905 to 1940.
Morris Fishbein, M.D., Editor, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Chicago.

(Subject to Be Announced.)
Irving S. Cutter, M.D., LL.D., Dean, Northwestern University Medical School, Chicago.

The Work of the National Board of Medical Examiners During Its First Quarter Century.
Louis B. Wilson, M.D., Director Emeritus, Mayo Foundation for Medical Education and Research, Rochester, Minn.

Program for the Instruction of Interns.
Nathan B. Van Etten, M.D., President-Elect, American Medical Association, New York; Nathan Davis, M.D., New York.

The Recognition of Professional Aims in the Teaching of the Fundamental Medical Sciences.
M. B. Visscher, M.D., Ph.D., Professor of Physiology, University of Minnesota Medical School, Minneapolis.

Role That a Children's Hospital Should Play in the Community.
Alan Brown, M.D., Professor of Pediatrics, University of Toronto Faculty of Medicine, Ontario.

Licensing the Professions.
Miss Frances P. De Lancy, Department of Political Science, West Virginia University, Morgantown.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

District Meetings.—At a meeting of the Third Councilor District Medical Society in Stuttgart October 26 the speakers included Drs. Clyde D. Rodgers, Little Rock, on "Puerperal Disorders in Obstetrics"; Silas C. Fulmer, Little Rock, "Hypertension"; William C. Chaney, Memphis, Tenn., "The Medical Man and His Neurologic Problems," and Henry T. Smith, McGehee, "The Future of Organized Medicine."——The Second Councilor District Medical Society was addressed in Searcy October 19 by Drs. Rufus B. Robins and Samuel A. Thompson, both of Camden, on "Some Remarks on Head Injuries" and "Heart Problems in the Smaller Centers" respectively. Dr. Albert S. Buchanan, Prescott, president of the state medical society, also spoke.—— The First Councilor District Medical Society was addressed at Paragould October 17 among others by Drs. Ralph M. Sloan, Jonesboro, on "Premature Separation of the Placenta"; Charles S. Paddock, Memphis, Tenn., "Pyelitis of Pregnancy," and Neuton S. Stern, Memphis, "Acute Angina."

CALIFORNIA

Personal.—Dr. Ruggles A. Cushman has retired as superintendent of the Mendocino State Hospital, Talmage; he served as assistant superintendent of the hospital from 1904 to 1910 and had been superintendent since 1932.

Society News.—At a meeting of the Riverside County Medical Association in Riverside recently Dr. William E. Gardner discussed "Obstructions in Urology."——Among others, Dr. Paul A. Gliebe, San Francisco, spoke on "Psychiatry and the General Practitioner" before the San Joaquin County Medical Society in Stockton recently.——Dr. Emile F. Holman, San Francisco, addressed the San Diego County Medical Society November 14 on "Arteriovenous Aneurysm, Experimental and Clinical Considerations."—— Dr. Anton S. Yuskis discussed "Embolic Manifestations of Heart Disease" before the San Diego Galen Club October 24.——At a meeting of the Los Angeles Surgical Society November 10 the speakers were Drs. Ralph T. Richards, Salt Lake City, on "Use of Oxygen and Carbon Dioxide in Surgery"; Verne C. Hunt, "Total Gastrectomy," and Lowell S. Goin, "Observations on Refrigeration Therapy for Malignant Disease."

GEORGIA

Special Society Election.—Dr. Robert L. Rhodes, Augusta, was recently elected president of the Georgia Industrial Surgeons' Association. Other officers are Drs. Richard E. Newberry, Atlanta, vice president, and John W. Simmons, Brunswick, secretary.

Personal.—Dr. Robert C. Pendergrass has been appointed director of a newly organized cancer clinic in Americus.—— Dr. Jack R. McMichael, Quitman, has been appointed a member of the state board of health.—— Dr. Clarence L. Ayers, Toccoa, has been appointed a member of the state board of health for a six year term.

Annual Pediatric Meeting.—The Georgia Pediatric Society will hold its annual scientific session in Atlanta December 16. The speakers will include Drs. George M. Lyon, Huntington, W. Va., on "Meningococcic Meningitis and Its Management" and "Purulent Meningitis Due to Other Than the Meningococcus"; Harry Bakwin, New York (subjects not announced), and Charles F. McKhann, Boston, "Poliomyelitis" and "Progress in the Control of Respiratory Infections." Dr. Lewellyn H. Muse, Atlanta, is president of the society and Dr. Don F. Cathcart, Atlanta, secretary-treasurer.

ILLINOIS

Society News.—Dr. Oliver E. Van Alyea, Chicago, discussed "Irrigation of the Frontal and Maxillary Sinuses" before the Rock River Valley Eye, Ear, Nose and Throat Society in Rockford November 21.——Dr. Frederick A. Jostes, St. Louis, discussed "Backache: A Manipulative Treatment Without Anesthesia" at a meeting of the Adams County Medical Society in Quincy November 13.

Chicago

New Position at Cook County Hospital.—Dr. Marshall Davison, chairman of the surgical division of Cook County Hospital, has been appointed medical director of the hospital, a newly created position. In this capacity Dr. Davison will coordinate and correlate activities of the staff and have jurisdiction over all medical and surgical work at the hospital. Dr. Karl Meyer will continue as medical superintendent. Dr. Davison graduated at the University of Illinois College of Medicine in 1920. He is assistant professor of surgery at Northwestern University Medical School.

INDIANA

Changes in Health Officers.—Dr. Wendell C. Anderson, Mentone, has been appointed director of the district health department, covering Dubois, Spencer, Orange, Crawford and Perry counties, with headquarters in Huntingburg. He succeeds Dr. Chester A. Hicks. Dr. Lewis C. Robbins, formerly of Baltimore, has been placed in charge of the district health unit covering Monroe, Brown and Lawrence counties, with headquarters in Bloomington. He succeeds Dr. Henry G. Steinmetz, who has received a fellowship in public health at Johns Hopkins University.

District Meetings.—At a meeting of the Thirteenth District Medical Society November 8, Laporte, Drs. Fred W. Bailey, St. Louis, among others, discussed diagnosis and treatment of nonpenetrating intra-abdominal injuries, and Edwin M. Miller, Chicago, treatment of severe fractures of the elbow in children.—— The Seventh District Medical Society was addressed in Martinsville November 15 by Drs. Carl P. Huber, Indianapolis, on "Toxemias of Pregnancy"; Maurice L. Blatt, Chicago, "Care of the Premature and Newborn Infant"; Robert M. Moore, Indianapolis, "Some Helpful Clinical Observations in Angina Pectoris"; Karl R. Ruddell, Indianapolis, "Acute Appendicitis." Dr. M. Herbert Barker, Chicago, addressed the dinner session on "Management of Pneumonia in Children and Adults."

KANSAS

Lectures on Medical History.—The Kansas University School of Medicine, in commemoration of the opening of its new library and museum of medical history, is presenting a series of lectures on medical history. Dr. Sanford V. Larkey, librarian of the William H. Welch Memorial Library, Johns Hopkins University School of Medicine, Baltimore, gave the first lectures October 9 on "Primitive Medicine" and "Egyptian Medicine." Other lecturers include:

Dr. John Farquhar Fulton, New Haven, Conn., January 15, History of Physiology.
Dr. Henry E. Sigerist, Baltimore, March 4, Methods of Medical History and the Future of Medicine in the Light of History.
Chauncey D. Leake, Ph.D., San Francisco, March 11 (date tentative), History and the Development of Therapeutic Drugs and the History of Anesthesia.

MARYLAND

University News.—Dr. Charles Edward Smith, associate professor of public health and preventive medicine, Stanford University School of Medicine, San Francisco, delivered a public lecture at the Johns Hopkins School of Hygiene and Public Health, Baltimore, November 7, on "Epidemiology of Acute Coccidioidomycosis with Erythema Nodosum ('San Joaquin' or 'Valley Fever')." This was one in the series of the De Lamar Lectures in Hygiene.

Society News.—A symposium on Rocky Mountain spotted fever was presented before the Baltimore City Medical Society November 3 by Drs. Thomas Nelson Carey, Charles H. Halliday and Rolla E. Dyer, U. S. Public Health Service. At a meeting November 17 Drs. Warfield M. Firor and George W. Thorn discussed "The Modern Treatment of Addison's Disease" and Dr. Edward S. Stafford, "Mortality from Appendicitis."——Dr. William S. Love Jr., Baltimore, discussed symptomatology, diagnosis and treatment of coronary thrombosis before the Harford County Medical Society in Bel Air recently.

Study of Hearing of School Children.—A study of selected school children to detect impaired hearing will be carried out in the Eastern Health District, according to Baltimore *Health News*. The work will be done under the supervision of Dr. Samuel J. Crowe, adjunct professor of laryngology and otology, Johns Hopkins University School of Medicine, Baltimore, and his staff in collaboration with city departments of education and health and the Eastern Health District. The study will involve careful examination, including

an audiometric test, of 1,000 or more school children between the ages of 8 and 12. When found necessary, arrangements for adequate treatment will be made after consulting and receiving approval from the children's parents and family physicians.

MASSACHUSETTS

Conference on Physical Medicine.—The New England Society of Physical Medicine held a clinical conference November 8-10 at Boston and the Massachusetts Institute of Technology, Cambridge, November 10. Among the speakers were:

Dr. Harold E. Himwich, Albany, N. Y., Nitrogen Therapy, Physiologic Aspects in Schizophrenia.
Drs. Charles W. McClure and Isaac R. Jankelson, Boston, Gastroscopy.
Dr. Temple S. Fay, Philadelphia, Observations on Human Refrigeration.
Drs. Curtis T. Prout, Arlington Heights, Mass., and John G. Gibson II, Boston, Fever Therapy.

There were symposiums on galvanism and the sinusoidal currents, high frequency currents, phototherapy and massage and corrective exercise. At the banquet, Harold E. Edgerton, Ph.D., discussed "Seeing the Unseen with Stroboscopic Photography" and George R. Harrison, Ph.D., "Modern Physics and the Modern Physician." Dr. Henry A. Tadgell, Wrentham, is president of the society and Dr. William D. McFee, Boston, secretary.

MISSISSIPPI

Society News.—The Northeast Mississippi Thirteen Counties Medical Society was addressed recently, among others, by Drs. James A. Watt, Aberdeen, on "Migraine, Its Present Day Concept and Treatment"; Claud F. Gilbert, Corinth, "Prenatal Care"; Luther L. McDougal Jr., Paris, Texas, "Feeding a Normal Infant," and Cecil D. Gaston, Birmingham, Ala., "Hemorrhoidectomy, Essentials in the Prevention of Postoperative Pain."

Health Department Activities.—Full time health departments will soon be established in Marion, Lowndes, Tate, Noxubee and Newton counties to bring the total of full time health units in the state to forty-four, newspapers announce. Dr. Robert H. Bostwick Jr., Indianola, has been made director of the Union County health department succeeding Dr. Edwin M. Butler, Liberty, who plans to enter private practice. Dr. James P. Ward, Charleston, director of Tallahatchie County, has been appointed director of the Washington County health department, effective October 15, succeeding Dr. Benjamin F. Hand Jr., who resigned to engage in private practice in Greenville, it is reported. Dr. Everett W. Ryan, Canton, formerly director of the Madison County health unit, is being transferred to Charleston to direct the Tallahatchie department.

MISSOURI

Personal.—Dr. Henry H. Sweets Jr., Louisville, Ky., has been appointed to the staff of the University of Missouri School of Medicine, succeeding Dr. James H. Peers, who recently resigned as assistant professor of pathology. —— Dr. Charles Wesley Burrill, Kansas City, said to be the oldest living member of the Jackson County Medical Society, was honored by friends October 21 in observance of his ninety-fourth birthday.

Society News.—At a meeting of the St. Louis County Medical Society November 22 the speakers were Drs. Peter Heinbecker on "The Surgical Treatment of Hypertension"; Nathan A. Womack, "Recent Advances in the Knowledge of Cancer," and Robert Elman, "Surgical Treatment of High Intestinal Obstruction in Infants."——Dr. William S. McCann, Rochester, N. Y., will address the Kansas City Academy of Medicine December 15 on "Modern Trends in the Study of Kidney Disease." Dr. Harold E. Himwich, Albany, N. Y., discussed "Brain Metabolism" before the academy November 17. —— Dr. Oscar V. Batson, Philadelphia, addressed the Kansas City Society of Ophthalmology and Otolaryngology December 7-8 during its postgraduate session on anatomy.

Neuropsychiatrist Honored.—A meeting of the St. Louis Medical Society October 24 was held in honor of Dr. William W. Graves, professor and director of the department of neuropsychiatry, St. Louis University School of Medicine, St. Louis. At this time he was presented with a certificate of merit and a gold medal. The award of merit points out that Dr. Graves' work "resulted in new approaches to the qualitative evaluation of inherited variations in relation to the inherited qualities of human constitution, expressed in inherited predisposition to health or disease, and in inherited capacity for education, for adaptability, and for longevity." The society has conferred this honor on only two previous occasions: In 1927 to Dr. Evarts A. Graham and his associates, Drs. Glover H. Copher, St. Louis, Warren H. Cole, now of Chicago, and Sherwood Moore, St. Louis, for their work in cholecystography, and in 1935 to Edward A. Doisy, Ph.D., for his achievements in hormone chemistry and physiology.

NEVADA

Changes in State Board.—New members of the Nevada State Board of Medical Examiners are Drs. Frederick M. Anderson, Carson City; John Vernon Cantlon, Reno, and George R. Magee, Yerington. Drs. Robert P. Roantree, Elko, and Ralph A. Bowdle, East Ely, continue as members. Dr. Roantree is president and Dr. Anderson is secretary.

NEW YORK

Personal.—Dr. John Maxwell Chamberlain, formerly of Ann Arbor, Mich., has been appointed principal thoracic surgeon on the staff of the division of tuberculosis in the state department of health, Albany.——Dr. James Bernard Lawler, Vernon, has been appointed health officer of the township except the city of Sherrill, succeeding Dr. Gary M. Lewis, who had served for sixty years except for a short period.

Society News.—Mr. J. George Crownhart, executive secretary, State Medical Society of Wisconsin, Madison, addressed the Medical Society of the County of Westchester at White Plains at its annual meeting November 21 on "Sickness Insurance in Europe."——Dr. Carl Eggers, New York, addressed the Medical Society of the County of Albany November 15 on "Carcinoma of the Breast."——Dr. John S. Lawrence, Rochester, addressed the Rochester Pathological Society November 14 on "Toxic Effects on the Blood of Sulfanilamide and Allied Drugs."——Dr. Walter C. Alvarez, Rochester, Minn., addressed the Rochester Academy of Medicine November 1 on "The Patient Who Remains Sickly in Spite of Long and Strenuous Treatment."——Dr. Jesse G. M. Bullowa, New York, addressed the Dutchess County Medical Society, Poughkeepsie, November 8 on "The Appropriate Treatment for the Pneumonias—Individualizing the Case."——Drs. John E. Free and Jay E. Meeker, Ogdensburg, addressed the Medical Society of the County of St. Lawrence in Potsdam November 2 on "Surgery of the Chest" and "Delivery of the Occiput Through a Presenting Cervix" respectively.

New York City

New Officers of Rockefeller Institute.—Dr. Warfield T. Longcope, Baltimore, was elected president of the board of scientific directors of the Rockefeller Institute for Medical Research at a meeting October 28. He succeeds the late Dr. Charles R. Stockard. Dr. Ross G. Harrison, New Haven, Conn., was elected a member of the board.

Society News.—A symposium on empyema was presented before the Brooklyn Thoracic Society November 24 by Drs. William H. Field, Henry W. Louria, Herbert C. Maier and Harry B. Reibstein.——At the first fall meeting of the International Spanish-Speaking Association of Physicians November 10 the speakers were Drs. Felipe Carranza, Buenos Aires, on "Treatment of Cancer of the Rectum"; Irving W. Potter, Buffalo, "Prevention of Maternal Deaths," and Nathaniel M. Levin, Philadelphia, "Speech Following Radical Removal of the Larynx."

Dr. Rose Honored.—Mary Swartz Rose, Ph.D., professor of nutrition, Teachers College, Columbia University, received the annual award of the Associated Grocery Manufacturers of America at the recent annual convention in New York. Dr. Rose was honored, the citation said, in recognition of her contributions to the science of nutrition, the part she has played in the dissemination of scientific information concerning foods, her authorship in this field and her outstanding career as a teacher of others who teach nutrition. Dr. Rose is a member of the Council on Foods of the American Medical Association.

Lectures to the Laity.—The New York Academy of Medicine began its fifth annual series of lectures to the laity November 30 with an address by Dr. Abraham Myerson, Boston, on "The Inheritance of Mental Disease." The series will continue as follows:

Dr. Richard H. Hutchings, Utica, N. Y., The Ascent from Bedlam, December 28.
Dr. Paul Rennikoff, New York, The Story of Our Knowledge of the Blood, January 25.
Drs. Chevalier Jackson and Chevalier L. Jackson, Philadelphia, The Romance of Bronchoscopy, February 29.
Dr. Thomas M. Rivers, New York, The Story of the Viruses, March 28.
Dr. Perrin H. Long, Baltimore, Chemical Warfare Against Disease, April 25.

Knapp Hospital Merged with Columbia.—Announcement is made of the merger of the Herman Knapp Memorial Eye Hospital with the Columbia-Presbyterian Medical Center. The hospital activities and care of patients now carried on by the Knapp Hospital at 500 West Fifty-Seventh Street will be taken over by the Presbyterian Hospital and the Vanderbilt Clinic. The hospital's assets and funds will be conveyed to Columbia and will be administered as the Knapp Memorial Foundation in Ophthalmology, the income of which will be used for graduate study, teaching and research in ophthalmology. The Herman Knapp Memorial Eye Hospital was founded in 1869 by Dr. Knapp as the New York Ophthalmic and Aural Institute. In 1909 Dr. Knapp was succeeded as executive surgeon by his son Dr. Arnold Knapp, and in 1913 the hospital became the Herman Knapp Memorial Eye Hospital with a new building situated near Columbia University College of Physicians and Surgeons. More than 800,000 patients have been treated at the hospital, 730,000 in the outpatient department and 70,000 inpatients, 76 per cent of whom were treated free, it was stated in the announcement. Dr. Herman Knapp was professor of ophthalmology at the University of Heidelberg, Germany, before he came to the United States in 1868. He died in 1911.

OHIO

The Annual Lower Lecture.—The second annual Lower Lecture of the Academy of Medicine of Cleveland was delivered November 17 by Dr. George H. Whipple, Rochester, N. Y., in the Cleveland Medical Library auditorium. Dr. Whipple's subject was "Hemoglobin Building in Anemia with Particular Reference to Iron."

Toledo University Institute.—The Sixth Annual Postgraduate Day of the Medical Institute of Toledo University was held November 3. The lecturers were Drs. Willard O. Thompson and Harry E. Mock, Chicago, who made three addresses each. Dr. Thompson's subjects were: "Treatment of Undescended Testes and Hypogenitalism," "Treatment of Addison's Disease" and "Treatment of Toxic Goiter." Dr. Mock's were: "Treatment of Injuries with Special Attention to Lacerations and Tendon Sutures," "Treatment of Shock" and "Treatment of Head Injuries."

Personal.—Dr. Elmer G. Horton, who recently retired as clinical professor and chairman of the department of pediatrics at Ohio State University College of Medicine, Columbus, was honored at a dinner October 19 attended by 270 Ohio physicians and guests. Mr. Horace S. Kerr, Columbus attorney, was toastmaster, and the speakers included William McPherson, LL.D., acting president of the university, Drs. Elijah J. Gordon, John W. Wilce and Harry E. LeFever.——Dr. William K. Ruble, Wilmington, health commissioner of Clinton County since 1921, has retired.——Dr. Albert Graeme Mitchell, Cincinnati, has been appointed a member of the committee on education of the National Foundation for Infantile Paralysis.

PENNSYLVANIA

Outbreak of Scarlet Fever.—Schools were closed November 14-27 in Chester because of an outbreak of scarlet fever. More than sixty cases had been reported up to November 16. Seven of the patients were adults.

Postgraduate Day in Harrisburg.—A Postgraduate Day was held at the Harrisburg Academy of Medicine, Harrisburg, November 16, with the following speakers:

Dr. Charles C. Higgins, Cleveland, Management of Patients with Renal Lithiasis.
Dr. Alexander H. Colwell, Pittsburgh, Intrathoracic Tumors.
Dr. Randle C. Rosenberger, Rahns, Interesting Facts Concerning Viruses and Viral Diseases.
Dr. George P. Müller, Philadelphia, Surgical Treatment of Peptic Ulcer.

After a dinner at the Harrisburg Country Club Dr. Colwell spoke on "The House in Order" and Dr. Rosenberger, "Students I Have Met, or Trials and Tribulations of a Teacher."

Philadelphia

Personal.—Detlev W. Bronk, Ph.D., director of the Eldridge R. Johnson Foundation for Medical Physics and of the Institute of Neurology, University of Pennsylvania School of Medicine, has been appointed managing editor of the *Journal of Cellular and Comparative Physiology* of the Wistar Institute of Anatomy and Biology. He succeeds Edmund Newton Harvey, Ph.D., Princeton University, Princeton, N. J.

Medical Economics and Health.—The Philadelphia County Medical Society held a "health and medical economics night" November 8 with the following speakers: Dr. John J. Shaw, state secretary of health, on "Activities of the Department of Health of the Commonwealth of Pennsylvania"; Hon. J. William Ditter of Montgomery County, "The Congressman Looks at the Doctor," and Dr. Arthur C. Christie, Washington, D. C., "The Physician's Responsibility for Medical Progress."

Annual Women's Cancer Forum.—The annual cancer forum under the auspices of the Women's Auxiliary of the Lankenau Hospital Research Institute was held at the Bellevue-Stratford November 28-29. The auxiliary was assisted by District No. 1 of the Pennsylvania State Nurses Association, with the cooperation of various health and medical organizations. Several groups presented exhibits on facts and research into the cancer problem. One session was devoted to seminars led by physicians interested in special phases of cancer. Among out of town speakers was Harold S. Burr, Ph.D., New Haven, Conn., on "Electricity in Cancer."

Pittsburgh

Hospital News.—Montefiore Hospital held its annual "Scientific Day" November 18 with Dr. Charles R. Austrian, Baltimore, as the guest speaker. Short papers and cases were presented at the hospital during the day and Dr. Austrian spoke in the evening at the Concordia Club on "Diagnosis and Treatment of Chronic Nontuberculous Pulmonary Infections."

Society News.—Speakers before the Pittsburgh Urological Association November 13 were Drs. Isaac L. Ohlman, on "Carcinoma of the Ureter"; David H. Ruben, Washington, Pa., "Carcinoma of the Ureter; Ten Year Cure" and Howard L. Tolson, Cumberland, Md., "Prostatic Resection with a Modification of Young's Punch."——At a meeting of the Pittsburgh Surgical Society November 17 the speakers were Drs. John W. Shirer on "Preliminary Report on Peritoneoscopy; A New Diagnostic Method for Diseases of the Abdominal Cavity"; Dominic N. Di Silvio and Morris A. Slocum, "A Survey of 695 Herniorraphies," and John W. Fredette, "Chronic Dislocations of the Shoulder Joint with Special Reference to Technic of Operation for Repair."

RHODE ISLAND

Changes in Hospital Superintendents.—Dr. Dennett L. Richardson has resigned as superintendent of the Charles V. Chapin Hospital, Providence, to become superintendent of the Rhode Island Hospital, Providence, effective January 1. Dr. Richardson will succeed Dr. William O. Rice, who has resigned to take up other work.

Society News.—Drs. Champ Lyons, Boston, and Samuel Morein addressed the Providence Medical Association November 6 on "Chemotherapy and Immunology of Pyogenic Infections" and "Newer Aspect of the Medical Treatment of Gastric and Duodenal Ulcers" respectively. Dr. Allen Greenwood, Boston, was the speaker October 2 on "Eye Diseases Related to General Medicine and Surgery."

Course in Psychiatric Nursing.—The Emma Pendleton Bradley Home, East Providence, announces a postgraduate course in the practical nursing care of neuropsychiatric disorders of childhood. The course will run through twelve weeks beginning the first of January, April, July and October and will be limited to two nurses for each period. Details may be obtained from Dr. Arthur H. Ruggles, superintendent; Dr. Charles Bradley, medical director, or Kathleen Thornton, R.N., director of nursing. The Bradley Home is a fifty bed hospital dealing exclusively with neurologic and behavior disorders of children under 13 years of age.

TENNESSEE

Monument to a Family Doctor.—A monument to the memory of Dr. William P. Moore Jr., Portland, Tenn., who served the community for about fifty years, was unveiled October 29. The memorial was erected through the contributions of his patients and friends and dedicated with an address by Dr. William D. Haggard, Nashville. Dr. Moore died in 1932, aged 75.

Personal.—Dr. Bedford F. Peterson, assistant superintendent of the Eastern State Hospital, Knoxville, has been appointed superintendent of the Western State Hospital near Bolivar, it is reported.——Dr. William D. Martin, head of the division of criminal insane at Central State Hospital, Nashville, has been appointed superintendent of the Eastern State Hospital, Knoxville; he succeeds Dr. Oscar S. Hauk, who was transferred to the central institution as superintendent.

Conference of Southern Pathologists.—The Sixth Conference of Southern Pathologists was held at the University of Tennessee College of Medicine, Memphis, November 20. The speakers were Drs. William R. Mathews, Shreveport, La., on

"The Aspiration Biopsy"; Charles W. Duval, New Orleans, "Teaching of Pathology and Bacteriology as One Subject Matter"; Oscar B. Hunter, Washington, D. C., "The Present Day Status of Clinical Pathology and Problems of the Clinical Pathologist," and Ernest W. Goodpasture, Nashville, unusual infections of the intestine. Orren W. Hyman, Ph.D., dean of the medical school, spoke at the luncheon, and the group was entertained at dinner by Dr. Harry C. Schmeisser.

Regional Meeting.—The Middle Tennessee Medical Association held its semiannual meeting in Springfield November 16 with the following speakers, among others:

Dr. Nathaniel S. Shofner, Nashville, The Factors of Safety in Thyroid Surgery.
Dr. Robert B. Gaston, Lebanon, Pelvic Endometriosis.
Dr. Albert Weinstein, Nashville, Experiences with the Use of Sulfanilamide in the Treatment of Undulant Fever.
Dr. Roscoe C. Kash, Lebanon, Observations on the Transmission of Infantile Paralysis.

TEXAS

Dallas Clinical Conference.—The Dallas Southern Clinical Society announces the following speakers for its twelfth annual Spring Clinical Conference to be held March 11-14 at the Hotel Adolphus:

Dr. Marion A. Blankenhorn, Cincinnati, medicine.
Dr. Chester S. Keefer, Boston, medicine.
Dr. Warren H. Cole, Chicago, surgery.
Dr. Frank E. Adair, New York, surgery, tumors.
Dr. Clay Ray Murray, New York, fractures, traumatic surgery.
Dr. John W. Harris, Madison, Wis., obstetrics and gynecology.
Dr. Meredith F. Campbell, New York, urology.
Dr. Frank E. Stevenson, Cincinnati, pediatrics.
Dr. Tracy B. Mallory, Boston, pathology.
Dr. Walter A. Fansler, Minneapolis, proctology.
Dr. Parker Heath, Detroit, ophthalmology.
Dr. Millard F. Arbuckle, St. Louis, otolaryngology, bronchoscopy.

District Meetings.—The Panhandle District Medical Society met recently in Lubbock with Dr. John W. Amesse, Denver, as guest speaker on the scientific program on "Diagnosis of the More Common Skin Affections in Infants and Children," and in the evening on "A Close-up of Dictators."——The Fourth District Medical Society held its annual meeting in Brady in October. Among the speakers on the scientific program were Drs. Oren H. Chandler, Ballinger, on "Liver Extract as a Therapeutic Agent"; Samuel Foster Moore Jr., San Antonio, "Newer Concepts in Estrogenic Therapy"; Victor E. Schulze, San Angelo, "Experiences in the Use of Sulfapyridine in Pneumonias," and Joseph F. McVeigh, Fort Worth, "Abnormal Cardiac Rates and Rhythms." Dr. Leopold H. Reeves, Fort Worth, president of the State Medical Association of Texas, spoke on "Present Day Problems of Organized Medicine" and Dr. Samuel E. Thompson, Kerrville, on "Socialized or Governmental Medicine."

WASHINGTON

New Health Officers.—Dr. Thomas H. Biggs, Chehalis, has been appointed district health officer for Grant and Douglas counties in Oregon and Dr. John B. Porter, formerly of Omaha, Neb., county health officer for Kitsap County to succeed Dr. Thomas C. Baldwin, Port Orchard.

State Health Survey.—Adolph J. Roth, Dr.P.H., formerly assistant professor of bacteriology and public health at Washington State College, Pullman, has been selected to conduct a health education survey under the auspices of the public health committee of the State Planning Council, according to *Northwest Medicine*. The survey is preliminary to establishment of health education recommendations for the public schools and state educational institutions.

WISCONSIN

Director of Mental Hygiene Appointed.—Dr. Gilbert E. Seaman, superintendent of the Winnebago State Hospital, has been appointed acting director of the division of mental hygiene in the new state department of public welfare established by the 1939 legislature. Morris G. Caldwell, Ph.D., Lexington, Ky., was appointed director of corrections.

Society News.—Drs. Willard L. Wood, Chicago, and Stanley J. Seeger, Milwaukee, addressed the Medical Society of Milwaukee County November 10 on "Arthritis" and "Some Technical Points in Pediatric Surgery" respectively.——A symposium on biliary surgery was presented before the Milwaukee Society of Clinical Surgery November 28 by Drs. Max Thorek, Chicago, and Armand J. Quick and William J. Carson, Milwaukee.

GENERAL

Sedgwick Medal Awarded to Dr. Parran.—The Sedgwick Medal, awarded annually by the American Public Health Association for distinguished service in public health, was presented at the recent annual meeting to Dr. Thomas Parran, surgeon general of the U. S. Public Health Service, Washington, D. C. The presentation was made by Dr. Milton J. Rosenau, director of the division of public health, University of North Carolina School of Medicine, Chapel Hill.

Congress on Pediatrics Postponed.—The American officers of the Fifth International Congress of Pediatrics, which was scheduled to be held in Boston Sept. 3-5, 1940, have decided that the international situation is such at present that it seems advisable to postpone the congress to an indefinite date. Dr. Henry F. Helmholz, Rochester, Minn., is president of the congress, Dr. Kenneth D. Blackfan, Boston, general secretary, and Dr. Charles F. McKhann, Boston, assistant secretary.

Radiological Society Meeting.—The annual meeting of the Radiological Society of North America will be held in Atlanta December 11-15 at the Atlanta-Biltmore Hotel, under the presidency of Dr. Raymond G. Taylor, Los Angeles. Refresher courses are to be conducted each morning throughout the week from 8:30 to 10:30. General sessions will be held in the mornings and separate sessions for diagnostic and therapeutic subjects in the afternoons. Dr. Francis Carter Wood, New York, will deliver the Carman Lecture Tuesday evening December 12 on "The Biological Effects of Radiation."

Infantile Paralysis Campaign.—The 1940 campaign for funds to fight infantile paralysis will again have two principal features, celebrations in honor of President Roosevelt's birthday, January 30, and the "March of Dimes," according to an announcement of the Committee for the Celebration of the President's Birthday. Mr. Keith Morgan, New York, is again national chairman and has appointed chairmen for all the states and territorial possessions. The celebrations will include dances, parties and entertainments of all kinds. A special feature will be the "March of Sports," a series of sports events under the general direction of Grantland Rice. The funds will be distributed on the same plan as last year, one half to the National Foundation for Infantile Paralysis and the other half to the localities where the money is raised.

Laboratory Directors Reorganize.—The Conference of Laboratory Directors, meeting during the annual convention of the American Public Health Association in October, changed its name and expanded under a new constitution and by-laws. The new name is Conference of State and Provincial Public Health Laboratory Directors. Full membership is limited to directors of official public health laboratories, while associate membership has been made available to the responsible assistants of directors of state and provincial laboratories and to the directors and responsible assistants in municipal and other official public health laboratories in the United States and Canada. Friend Lee Mickle, Sc.D., Wethersfield, Conn., was elected president; Mr. L. F. Ey, Columbus, Ohio, vice president, and Miss Katherine E. Cox, Charleston, W. Va., secretary.

Special Society Elections.—Dr. Gerald H. McMahon, Detroit, was elected president of the International Association of Police and Fire Surgeons and Medical Directors of Civil Service Commissions at the eighteenth annual meeting in New York in October. Dr. William M. Doody, Jersey City, N. J., was named vice president and Dr. John J. White, New York, secretary.——Dr. H. Earle Conwell, Birmingham, Ala., was elected president of the Clinical Orthopaedic Society at its recent annual session in Oklahoma City and Little Rock, Ark. Dr. Conwell was formerly secretary-treasurer of the society. Other officers are Drs. Charles A. Stone, St. Louis, vice president, and Myron O. Henry, Minneapolis, secretary-treasurer. The next annual session will be held in Milwaukee and Madison, Wis.——Dr. Jennings C. Litzenberg, Minneapolis, was elected president of the Central Association of Obstetricians and Gynecologists at the annual meeting in Kansas City, Mo., in November. Drs. Thomas B. Sellers, New Orleans, and Edward P. Allen, Oklahoma City, were elected vice presidents and Dr. William F. Mengert, Iowa City, secretary. The 1940 convention will be in Indianapolis.——Dr. Leon Banov, Charleston, S. C., was chosen president of the International Society of Medical Health Officers at the annual meeting in Pittsburgh October 16; other officers are Drs. James R. Roberts, Hamilton, Ont., Canada, and Angel de la Garza Brito, Mexico City, vice presidents, and Dr. Irl C. Riggin, Richmond, Va., secretary-treasurer.

V 113
1939

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 4, 1939.

The Treatment of Air Raid Casualties

The organization for the treatment of the large number of air raid casualties expected among civilians has been described in previous letters. As no such raids have occurred we have had no experience with the arrangements, but the recent civil war in Spain seems to show that some modification is desirable. A well attended meeting of the Royal Society of Medicine was addressed by Dr. Trueta, formerly director of the department of surgery of the General Hospital of Catalunya, Barcelona, on the organization of hospital services for casualties due to the bombing of cities. He said that the numerous air raids on Barcelona had led the medical authorities to alter their organization as experience demanded. When it was found that first aid posts separate from the hospitals delayed complete treatment and increased mortality, they were abandoned. The wounds caused by the explosion of heavy bombs were severe and only few of the injured survived. Transportation was difficult, for movement increased shock and hemorrhage. Dispatch to the nearest hospital for complete treatment was the only measure that could save life. Those injured in the collapse of buildings from explosions also needed immediate assistance and even then the mortality was high. Persons should receive hospital treatment within two hours of the injury. Trueta strongly urged that first aid posts should be located in the hospitals. More than 30 per cent of the patients needed operation, and whatever facilitated rapid admission to a hospital contributed to success. The immediate intervention of the surgeon was the only useful form of first aid other than the application of a tourniquet for excessive bleeding. The application of splints, bandages and other forms of first aid at isolated posts was not only useless but dangerous because it delayed surgical treatment. A perfect circulation of ambulances was nesessary. The casualties should be classified into five groups: (1) those who required immediate operation and who could not be sent out immediately; (2) those who required immediate operation and could be evacuated immediately; (3) those who needed immediate treatment and rest without operation and could not be evacuated; (4) those who after first aid could be transferred to the base hospital; (5) those who could go home after first aid.

In the classification room a colored card should be attached to each injured person. The director of the classification unit should know the number of surgeons and operating tables available and the specialty of each, so that the cases might be distributed according to capacity and with some regard to the pressure on each operator. Trueta's address made a great impression. It was thought that his principles would revolutionize treatment in air raid casualties.

Dispensing with Foreign Pharmaceutic Products

Many of the pharmaceutic products used in this country are of foreign origin, especially German. We must now depend on our own resources, which are greater than has been generally realized. During recent months, steps have been taken to meet any possible deficiency. The Association of British Chemical Manufacturers has published a long schedule showing that a British product equivalent to almost every foreign one is available. This should not be difficult, as most of the extensively advertised foreign preparations are only chemical substances masquerading under a proprietary name. The British ones are claimed as having the same essential composition as the foreign or as having similar therapeutic properties and capable of replacing the foreign products. One firm has made arrangements to obtain supplies manufactured in the United States when its present foreign supply, which is considerable, has been exhausted.

Hospital for War Blinded Men

Before the outbreak of war it was decided at a conference between representatives of the fighting services, the Ministry of Pensions and the Ministry of Health to convert the convalescent home of St. Dunstan's Hospital into a war hospital for those who may be blinded in the present war. St. Dunstan's is known throughout the world for its care of those blinded in the great war. It was founded by Sir Arthur Pearson, a journalist who had become blind. The new hospital is situated on the downs near Brighton and has accommodations for 200 cases. It contains a small but perfectly equipped operating room in a part of the hospital erected at a cost of $35,000, thanks to the generosity of Lord Nuffield. A staff from Moorfields, the principal ophthalmic hospital in the empire, is in residence. Plans are in hand to extend the hospital, if the need arises, and to enlarge the present school so that all the young blinded men may learn to read with their fingers, to typewrite, to look after themselves and to walk alone. The blinded men of the great war will hold out a helping hand to the young men who will join their ranks and take an active part as lecturers and teachers. There will be workshops and lecture rooms where trades, handicrafts and professions will be taught. The government will provide pensions for those blinded in the war and, as in the last war, St. Dunstan's will help them to recreate their lives. Of the 2,750 who were treated here, 2,000 are still alive.

The Evacuation of Sanatoriums for Tuberculosis

The council of the National Association for the Prevention of Tuberculosis has called attention to the danger of the evacuation of sanatoriums and hospitals for tuberculosis, which has taken place all over the country as part of the scheme to provide hospitals for the wounded. The patients have been distributed in their homes and many of them are infective to others. The council says that an infective case of pulmonary tuberculosis may in time cause as much harm as a bomb. Cases are known in which, after previous warning, a sanatorium has been evacuated at forty-eight hours' notice, and the council asks whether many of the beds might not still be used for tuberculous patients and evacuation done when the necessity arises. Another point is that tuberculosis will undoubtedly occur in members of the fighting forces, for whom sanatoriums should be available to the greatest possible extent.

PARIS

(From Our Regular Correspondent)

Oct. 29, 1939.

The Prognosis in Chronic Ascites

Cirrhotic ascites is rarely curable. Cases regarded as cures are generally remissions of long duration. Kervarec recently described before the Société de médecine de Paris the case of a woman aged 50 suffering from hypertrophic cirrhosis with ascites and enormous edema. She had undergone fifty-four punctures within eighteen months, in the course of which 779 quarts of peritoneal fluid were drained. The ascites had not reappeared for nine years. She had pneumonia in 1935 but in spite of hypertension (230/130) her condition was satisfactory. The prognosis of recent cirrhosis is more favorable than that of older cases, and the hypertrophic type heals more frequently than the atrophic. Icterus seriously aggravates the situation. Three kinds of symptoms signify the cure or evolu-

tion of ascites: First, the more or less rapid disappearance of portal hypertension is a factor which permits an improved outlook. Furthermore, the restoration of a normal relation between the blood serum and erythrocytes indicates a return to equilibrium in protein metabolism. In the third place, biologic tests show the persistence of hepatic insufficiency even after improvement that looks like a cure. Maillard's coefficient (Lanzenberg's acidosis coefficient) and urobilinuria remain quite high. On the other hand, experimental tests for galactosuria remain satisfactory.

The Rickettsias

In a recent session of the Société de pathologie exotique Paul Giroud and R. Pauthier reproduced specimens of conjunctival cells in which it was difficult to distinguish the Rickettsias of classic morphology from the bacteria modified by phagocytosis, clearly a potential cause of error for those who study the connection between trachomas and Rickettsias. At the same meeting Etienne Burnet voiced his skepticism of the role the Rickettsias play in the study of trachomas. He believes that the trachoma agent is a corpuscular virus of the same type as those of psittacosis and acute lymphogranuloma, a point of view derived from the descriptions of Halberstadter and Prowasek. The recently described Rickettsias cannot be accepted, at least as Rickettsias. They differ too much from the micro-organisms for which this name was coined. Either they are not Rickettsias at all or they belong to a species other than those whose presence in typhus has been ascertained. Weigl, on the other hand, has proved that Rickettsias of the type of rocha limae have nothing to do with trachoma. The transmission of "Rickettsia-like bodies" recently achieved by Cuénod and Nataf from louse to louse or from louse to man and monkey seems to indicate that these bodies, whatever name they should bear in the nomenclature, are indeed trachoma agents (THE JOURNAL, November 25, p. 1977).

BERLIN

(From Our Regular Correspondent)

Nov. 4, 1939.

Strangulation of Intellectualism

The "scientific academies of the national socialist alliance of German university instructors" constitute the chief weapon which the national socialist party has created to transform the universities. The three existing academies of this kind, in Göttingen, Kiel and Tübingen, recently held their annual session in Munich, "capital of the movement," as it is now officially designated. Dr. Schultze, its leader, who was previously unknown, declared that "the alliance is the appointed trustee of the national socialist party at the universities to see that universities and scholarship are not only painted brown but really made over to fit the pattern of national socialism." In the official opening address of the Bavarian government, the demand was made that "scholarship should serve life and that the national socialist party was today's life. Whatever stood aloof from it was doomed to die and be destroyed, even if still arrayed in ostentatious garments." Schultze had also this to say: that the present struggle of scholarship was to liquidate the ideas of a defunct past generation that had corrupted German thinking. All dominant ideas of the past, medieval dogmatic theology as well as the rationalism of the Enlightenment, had one thing in common; namely, they were of foreign origin. In the middle ages the Germans had learned to feel fear; the Enlightenment, on the other hand, had merely supplied the new ideas of equality and freedom, the former contrary to nature, the latter knowing no restraint. German scholarship, he said, had failed the people because it had emphasized objectivity so much that race, life, country and "weltanschauung" had been lost sight of. The German university of the last years was not to be compared with that of former years. He concluded with the statement that "German scholarship and German universities would become either thoroughly national socialist or cease to exist."

Another glimpse into how German cultural life is molded and reconstructed to serve Nazi purposes can be caught from Goebbel's remarks in keeping with his recent utterances on the "intellectuals." He delivered a speech in Berlin's palace of sports on the occasion of a district student gathering, in which he discussed the relation of the intellectual worker to the people and, in particular, the distinction between intelligence and intellectualism. He inveighed against the intellectualist, meaning, chiefly, university teachers and specialists who did not sufficiently bend the pregnant hinges of their knees to naziism, in whom reason had overgrown character and knowledge had destroyed faith. He called them "strolling scholars of our social life," representing not the upper ten thousand but the lower ten thousand, against whom one had to protect oneself. Perhaps it is, he said, the highest political duty to obey faithfully even when reason and knowledge from the point of view of the individual directs a different course. Of course, many of the older generation would regard this demand as impossible. However, the majority of the German people already possessed this discipline. German students should consider it their great political obligation to help achieve the fulfilment of this ideal. Intellectualism would then die a natural death. It was the duty of every intellectual worker, as of every other German, to obey Hitler. Utterances such as these by men high in the council of the totalitarian party on cultural life and the universities naturally affect also physicians and the pursuit and practice of medicine.

Control of the Use of Alcohol and Tobacco

The fight on alcohol and tobacco has been repeatedly reported in these columns (see THE JOURNAL, August 3, p. 1144). Lack of uniform regulations seems to have made necessary the creation of a "government bureau against the dangers of alcohol and tobacco," the administration of which was assumed by Dr. Conti, government health leader. It takes over the functions discharged previously by the government work union for combating alcoholism and by the organizations associated with it. The new bureau will also deal with the control of opiates and hypnotics. Its activities will include publicity and propaganda, the training of workers, the support of the internal administration of the related bureaus and the systematic organization and guidance of activities in relation to all persons who are ill and endangered. Furthermore, the bureau is to promote the production of sweet cider and all nonalcoholic beverages.

The regulation has been put in force recently in Germany prohibiting, in the advertising of tobacco merchandise and alcoholic beverages, reference in any form or fashion to what might create a public impression that hygienic values were connected with the use of tobacco and alcohol. Smoking is prohibited in government bureaus; similar prohibitions concern the army. Moreover, the head of Berlin's police department has requested automobile drivers to refrain from smoking because it increases traffic hazards. This police order will create criminal negligence for drivers who are involved in a collision while engaged in smoking.

According to official statistics, the consumption of beer increased in 1938 by about 4,250,000 hectoliters (1 hectoliter equals 26.4 U. S. gallons) to a total of 46,940,000 hectoliters, equivalent to a per capita increase from 62.9 to 68.8 liters, and the consumption of brandy by 65,000 hectoliters to a total of 827,000 hectoliters; that is, to 1.21 liters per capita of population. In general the increased buying power on the part of the public was accompanied with increased consumption of stimulants. The use of cigarets rose from 609 to 676 per

capita, that of coffee from 2.1 to 2.3 Kg. A decrease was noticed only in the consumption of wine, after the considerable surplus of the record vintages of 1934 and 1935 had been gradually consumed.

Prophylaxis Against Infection in Children's Homes

New directions have been officially released for the more effective protection of children sent away for recreational purposes. Before children are admitted in recreational homes or in private families they are to be medically examined twice, once about two months, the second from one to two days, before departure. At the same time, active vaccination against diphtheria of all children is recommended, the first about two months, the second a month before departure. Immediately on arrival the children should again be medically examined. All suspected children should be segregated until clarification of the diagnosis. Furthermore, all children are to be examined at least once a week during this vacational sojourn by a physician or a trained assistant for infectious diseases. The same precautionary examinations apply to the personnel of the homes and must be performed once every four weeks.

Students Conscripted into Harvest Fields

German students had to work in the harvest fields this year. The universities shortened the summer semester to enable the harvesting for the benefit of the eastern section of the country. The work period lasted from four to six weeks. All students had to serve no matter in what semester they were enrolled or for what course of studies they were registered. The only exemption allowed was the need of urgent preparations for an examination or some similar necessity. As Dr. Scheel, student leader for the reich, declared in his proclamation, it was the duty of German students to help secure their daily bread and make secure their frontiers and to feel enthusiasm for the führer and the German people. Every student was furnished with a work certificate, which he had to present when enrolling for the winter semester. Female students had to assist farm women or conduct harvest kindergartens for young children of peasants in the day time, while their parents were at work. At the end of July, 46,000 students were engaged in eastern Germany in agricultural or harvest work. They were protected by sufficient insurance against sickness and accidents.

Statistics of the Sick Funds

At the suggestion of the reich's public health department, a uniform system of voluntary statistics has been organized for the sick funds. The statistical department of the reich has just published the first results covering the year 1937. Eighty-seven sick funds, with a membership of 4,380,000, reported 1,090,000 male and 680,000 female illnesses. Exclusive of accidents and injuries caused by external agencies, the diseases of men that involved inability to work and loss of working days appeared in the following frequency: influenza 9.1 per cent, muscular rheumatism 5.1 per cent, bronchitis 4.4 per cent, furuncles, abscesses and so on 3.8 per cent, gastric diseases exclusive of ulcers 3.6 per cent, gastric and duodenal ulcers 3.4 per cent, organic cardiac diseases 3.2 per cent. Influenza, accounting also in the case of women for the greatest loss of working days, is represented by 9.6 per cent. Next in order are tonsillitis, pharyngitis and kindred inflammations with 4.5 per cent, organic cardiac diseases with 3.8 per cent, bronchitis with 3.5 per cent and neurasthenia and neuroses with 3.4 per cent.

Medical Training and Appointments

As reported in THE JOURNAL April 8, page 1401, a new medical curriculum has been decreed. Corresponding regulations governing appointments have now likewise been issued. Medical education has been reduced from eleven to ten semesters. The so-called practical year, which one had to serve after completing the final examinations in order to secure an appointment, has been abolished, effective April 1, 1940. The training course is now organized as follows: It begins with a course of six months attending and nursing patients before beginning university studies. The purpose is to eliminate the unfit. Preclinical studies follow in order and continue through four semesters. Successful completion is evidenced in preliminary examinations covering zoology, botany, chemistry, physics, anatomy and physiology. During the vacation periods of the two years the student must work six weeks either in a factory or on a farm. Clinical studies last six semesters. During the vacations, medical students are required to serve twice for three months each as hospital attendants. Provisions have been made so that students may take the state examination within four weeks (formerly it occasionally took six months). On passing the state examination, one is at once granted an appointment. The right to private practice is not allowed, however, until the young physician has served an obligatory year of internship in a hospital and a fourth of a year as assistant or substitute of a sick physician with a rural practice. Students unable to bear arms and female medical students must serve in the German Red Cross or do health welfare work in connection with the Hitler youth movement.

Organization of Committee to Combat Rheumatism

Professor Reiter, president of the public health department of the reich, has organized a committee of specialists to plan measures for protection against rheumatic diseases. Special attention is to be given to the early treatment and timely care of rheumatic persons. It is planned gradually to create effective organizations throughout the nation.

AUSTRALIA

(From Our Regular Correspondent)

Nov. 8, 1939.

Control of the Flying Doctor Service

The Australian Inland Mission Board of the Presbyterian church recently handed over control of the "flying doctor" services at Cloncurry (Queensland) to the Australian Aerial Medical Services. Queensland is the last of the states to register an association not for profit to form a link in a chain of aerial medical services conducted by this organization throughout Australia. The "flying doctor" scheme, as developed originally by the Australian Inland Mission at Cloncurry, is now well established as the most efficient way in which our "outback" settlers may be brought within reach of medical aid. Its development will stand for all time as a monument to Rev. John Flynn, whose dream it was. He realized the terrible isolation when illness or accident overtakes these people. He was familiar with the tragic stories of infants who had died in their mothers' arms on the heart breaking journey of hundreds of miles to the nearest doctor; of the men who, gravely injured in the course of their work, were faced with death where they lay from lack of skilled attention or being killed by the awful journey to a hospital over rough bush tracks. He realized how men shrank from the risk of taking a wife and children out there, with the result that much of our outback is inhabited by men alone. Without the influence of white women and children there seems inevitably to be a decline in those cultural and moral standards which are essential to satisfactory permanent settlement of our back country.

Mr. Flynn's inspiration to use an airplane as a means of transport and wireless as a means of communication between these outback people and their doctor is well known. The amazing thing about it is the clarity of that inspiration, conceived at a time (about 1912) when airplanes were unreliable and unsafe and wireless sets—especially transmitters—were hopelessly expensive and intricate. The airplane was improved

by commercial enterprise, and after years of experiment the wireless problem yielded to the genius of Alfred Traeger, encouraged and supported by Mr. Flynn and the Australian Inland Mission. At last in May 1928 the first aerial medical service base at Cloncurry, was formed. Since that time the Cloncurry base has gone forward steadily, meeting and conquering its difficulties as they arose and building up a tradition of service which holds the admiration of all who know it. It was found that the Cloncurry base could efficiently cover an area of 400 miles radius, that is, an area almost as large as New South Wales. So vast, however, is the sparsely settled part of Australia that there still remained thousands of isolated settlers far beyond the range of the mantle of safety spread by that base. It was obvious that at least six bases would be necessary to serve the whole of Australia's frontiers. A larger organization of national character was therefore formed to undertake the establishment of these bases. It was christened "Australian Aerial Medical Services." Under its auspices other bases have come into being and much valuable work has already been done in those areas.

The heart of an aerial medical service base is the mother radio station, situated close to the flying doctor's home. These stations are fairly powerful and send out excellent signals in voice so that the outback people listen to it just as easily as one does to a broadcast program. Scattered round the mother station are numerous pedal sets, the ingenious "transceivers" invented and built by Mr. Traeger. These small stations derive their main power from a generator driven by bicycle pedals and with them the owners are able to send clear signals in voice from distances of 700 miles and more. They have in reserve a remarkable instrument called an automatic transmitting keyboard for sending Morse code when atmospheric conditions are not suitable for voice. They are all thus kept in constant communication with the mother station and the doctor. Constantly at the disposal of the doctor is an airplane especially adapted to carry a patient on a stretcher in the cabin. The ambulance plane also carries wireless and so keeps the doctor in touch with his base and the rest of his large "practice" while he is out on a flight.

Several avenues of service are available with such organization: 1. Detailed advice as to treatment not only sets anxious hearts at rest in cases of minor illness but, when applied early, often prevents a major illness from developing. 2. A prompt call to the doctor, early diagnosis and quick, comfortable transport to a hospital, where efficient treatment can be given, are saving several lives each year in each of the areas now covered by the Aerial Medical Service. 3. Not the least valuable of these avenues involves no active work at all. The very presence in the district of the Aerial Medical Service base, able and willing to help in time of need, brings the outback people a sense of security hitherto unknown to them. 4. Wireless has broken down the isolation of the bush. Lonely women who do not see another white woman for months at a time can now converse in voice with their next door neighbor a hundred miles away. The receivers are used to receive broadcast programs and bring the news of the world to the most remote homes in the continent.

The Aerial Medical Service is rapidly developing in the back country a network of efficient communication and aerial transport facilities, such as landing ground and gasoline supplies—an interesting by-product of the purely medical work which is its mainspring.

Hydatid Disease in New Zealand

For nearly fifty years Sir Louis Barnett, emeritus professor of surgery, University of Otago, and chairman of the New Zealand Hydatid Research Committee, has concerned himself with an investigation of the high prevalence of hydatid disease in New Zealand. Now he has published in the *New Zealand Medical Journal* a further report on the incidence of the disease and the progress of the prevention campaign. The figures for 1938 are slightly better than those for 1937, but it is not yet permissible to claim a definite diminution of hydatid incidence in New Zealand. Last year the Hydatid Registry recorded a total of 1,304 cases with 151 deaths in a population of 1,604,244. In 787 cases the site of the cysts was the liver, and in 260 the lungs were involved. The prevalence of hydatid cysts in farm animals, as shown by abattoir tables and field research observations, continues at an alarming height. In New Zealand there are approximately 31 million sheep and 4¼ million cattle. Barnett claims that more than half of those reaching adult life have their livers and lungs studded with cysts either of Echinococcus or Tenuicollis type or both. The prevalence of the adult hydatid worm (Taenia echinococcus) in the dog is also considered very high.

The prevention campaign has been intensified during the year, and notable advances have been made in the lecturettes, films, models and specimen demonstrations at most of the Agricultural Shows and at other suitable gatherings. Another move that has this year focused the attention of dog owners on the subject of hydatid disease, its prevalence and ill effects and its possible prevention, is the distribution by the government to all dog owners in the dominion, on the occasion of dog registration, of a supply of arecaline vermifuge tablets, which can be depended on, if properly used, to eradicate not only the hydatid parasite but also sundry other worms to which dogs are prone.

Reports on the results of this action have been almost universally favorable but, as was only to be expected, there have been adverse comments receiving much attention in the press. These allegations, although unwarranted, have increased the number of dog owners who refuse or neglect to dose their dogs. At present they are under no legal obligation to do so; but the Hydatid Research Committee strongly urges that the two absolutely essential procedures in the campaign of hydatid eradication should be made compulsory by law. These procedures are (1) the regular administration of an approved vermifuge to all dogs and (2) the prohibition against the feeding of dogs on the raw livers and lungs of sheep and cattle.

Through the medium of the Hydatid Registry of the Royal Australasian College of Surgeons, clinical research on the problem of hyatids in Australia and New Zealand is also making headway, and with helpful cooperation from the community it should soon be possible to have the disease under efficient control.

Marriages

EUGENE AMOS HOLLAND to Miss Mary Frances White, both of Fairmont, W. Va., at Hot Springs National Park, Ark., August 17.

JOHN WILLIAM DINCOCT, Shelbyville, Tenn., to Miss Joy Carrier at Mortons Gap, Ky., October 7.

SAMUEL EUGENE FIELD, Centreville, Miss., to Miss Mildred Elizabeth Ruoff of Jackson, October 27.

MICHAEL D. MASSENGILL JR. to Miss Mary Linda Rector, both of Kingsport, Tenn., October 8.

BEN BESHOAR, Trinidad, Colo., to Mrs. Olive Waldrip of Los Angeles at Raton, N. M., October 3.

CARL FREDERICK NEUHOFF to Miss Hazel Louise Davenport, both of Peoria, Ill., October 14.

JULIA S. MEHLMAN to Maj. Frederick W. Greenhut, both of New York, November 11.

WIXOM S. SIBLEY to Miss Katherine Pickett, both of San Francisco, November 9.

NATHAN J. DAVIDOV to Miss Elsie Zerwitz, both of Baltimore, September 27.

JOHN R. MOODY to Miss Kathaleen Daniels, both of Erwin, Tenn., October 14.

Deaths

Charles Clifton Browning, San Marino, Calif.; University of Missouri School of Medicine, Columbia, 1883; member of the California Medical Association; professor emeritus (tuberculosis) at the College of Medical Evangelists, Loma Linda; fellow of the American College of Physicians; for many years a director of the National Tuberculosis Association; member of the American Clinical and Climatological Association; past president of the California Tuberculosis Association and the Los Angeles County Medical Association; served during the World War; formerly chief of the staff of the tuberculosis service, Los Angeles County Hospital; aged 78; died, September 28, of pneumonia.

Ashley Walker Morse ● Butte, Mont.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; for many years secretary of the Montana Academy of Oto-Ophthalmology; past president of the Silver Bow County Medical Society; consultant to St. James Hospital; aged 56; died, October 12, at Lansing, Mich., of pneumonia.

David Baker ● Colonel, U. S. Army, retired, Waltonville, Ill.; Barnes Medical College, St. Louis, 1893; fellow of the American College of Surgeons; veteran of the Spanish-American War; was commissioned an assistant surgeon in 1898, a captain in the medical corps of the U. S. Army in 1903 and rose through the various ranks to that of colonel in 1917; retired in 1935 by operation of law; aged 68; died, September 8, at Fort Sam Houston, Texas.

Jacob Usry Ray, Woodstock, Ala.; University of Tennessee Medical Department, Nashville, Tenn., 1893; member of the Medical Association of the State of Alabama and formerly treasurer; for many years secretary of the Alabama Association of Railroad and Industrial Surgeons; at one time postmaster; past president of the Bibb County Medical Society; aged 75; died, October 5, of myocarditis, arteriosclerosis and hypertension.

Howard Brownlee Hamilton ● Omaha; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; professor emeritus of pediatrics at the University of Nebraska College of Medicine; past president of Omaha-Douglas County Medical Society; member of the American Academy of Pediatrics; aged 64; died, October 12, of bilateral bronchopneumonia.

Bayard G. Keeney ● Shelbyville, Ind.; Medical College of Ohio, Cincinnati, 1902; fellow of the American College of Physicians; past president and secretary of the Shelby County Medical Society; health officer; for many years member of the city board of education; aged 63; died, October 11, at Fort Wayne of coronary occlusion while attending the state medical meeting.

Francis Washington Sovak ● New York; University and Bellevue Hospital Medical College, New York, 1911; clinical professor of obstetrics and gynecology at his alma mater; fellow of the American College of Surgeons; on the staffs of the Bellevue Hospital and the Misericordia Hospital; aged 54; died, October 27, in the Midtown Hospital.

Archibald Ray Knode ● Omaha; University of Nebraska College of Medicine, Omaha, 1904; formerly associate professor in the department of otorhinolaryngology at his alma mater; member of the American Academy of Ophthalmology and Otolaryngology; on the staff of the Immanuel Hospital; aged 57; died, October 11, of coronary thrombosis.

George Joseph Waggoner ● Ravenna, Ohio; University of the City of New York Medical Department, 1890; past president and secretary of the Portage County Medical Society; formerly member of the city board of health; on the staff of the Robinson Memorial Hospital; aged 74; died, October 7, of pulmonary thrombosis.

Wilbert Arthur Hobbs ● East Liverpool, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1884; fellow of the American College of Surgeons; Spanish-American War veteran; aged 77; on the staff of the East Liverpool City Hospital, where he died, October 17, of cerebral hemorrhage.

Austin Funk ● Jeffersonville, Ind.; University of Louisville (Ky.) Medical Department, 1900; served during the World War; formerly secretary of the Clark County Medical Society; aged 65; died, October 24, in the Clark County Memorial Hospital of skull fracture received in an automobile accident.

Oscar Brunk Funkhouser ● Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; Northwestern University Medical School, Chicago, 1909; aged 53; died, October 17, in the Washington Boulevard Hospital of mitral insufficiency.

Robert H. Trimble, Mount Sterling, Ohio; Starling Medical College, Columbus, 1894; member of the Ohio State Medical Association; county health officer; formerly mayor; past president of the school board; aged 69; died, October 18, in the Grant Hospital, Columbus, of carcinomatosis.

Fred Lawwill Rhodes, Massillon, Ohio; Ohio State University College of Medicine, 1916; served during the World War; formerly on the staff of the Massillon State Hospital; aged 49; died, October 10, in the White Cross Hospital, Columbus, of obstruction of the esophagus.

Harry Obadiah Knight ● Galveston, Texas; University of Texas School of Medicine, Galveston, 1907; member of the American Association of Anatomists; professor of anatomy at his alma mater; aged 58; died, October 5, in the John Sealy Hospital of a self-inflicted bullet wound.

Charles Edward Miller, Muncie, Ind.; Miami Medical College, Cincinnati, 1898; member of the Indiana State Medical Association; past president of the Delaware-Blackford Counties Medical Society; aged 69; died, October 17, of bronchopneumonia and heart disease.

Ralph Edgar Weller, Electra, Texas; University Medical College of Kansas City, Mo., 1904; member of the State Medical Association of Texas; fellow of the American College of Surgeons; served during the World War; aged 67; died, October 12, of cerebral hemorrhage.

Eugene Carl Roemele, Frankfort, Ky.; Hospital College of Medicine, Louisville, 1897; member of the Kentucky State Medical Association; county health officer; at one time medical director of the State Reformatory; aged 62; died, October 14, of angina pectoris.

James Buchanan Lightfoot, Miami, Okla.; Memphis (Tenn.) Hospital Medical College, 1905; member of the Oklahoma State Medical Association; aged 75; died, October 5, in the Miami Baptist Hospital of arthritis following an injury received in a fall.

Eugene Frederick Hauck, Clayton, Mo.; St. Louis Medical College, 1880; member of the Missouri State Medical Association; for many years medical director of St. Louis Mutual Life Insurance Company; aged 82; died, October 8, of pyelitis and heart disease.

Jacob John Minke, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; served during the World War; physician in chief to the Oak Forest (Ill.) County Infirmary; aged 56; died, October 1.

George Elias Boulos, Hazard, Ky.; University of Louisville (Ky.) School of Medicine, 1927; on the staff of the Hurst-Snyder Hospital; aged 36; was found dead, October 20, at his office in Louisville of illuminating gas poisoning, self administered.

Edwin Merville Bennett, Paris, Ill.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; member of the Illinois State Medical Society; served during the World War; aged 72; died, October 14, of coronary thrombosis.

Reuben Harrison Mast ● Myrtle Point, Ore.; University of Oregon Medical School, Portland, 1924; medical director of the Mast and Wilson Hospital; aged 44; died, October 8, as a result of an accidental fall from a hotel window in Portland.

Granville E. Dickinson ● Upper Fairmount, Md.; University of Pennsylvania Department of Medicine, Philadelphia, 1874; an Affiliate Fellow of the American Medical Association; aged 87; died, October 14, of acute dilatation of the heart.

Moza West Hurt, Mayfield, Ky.; University of Louisville (Ky.) Medical Department, 1911; member of the Kentucky State Medical Association; on the staff of the Mayfield Hospital; aged 54; died, October 6, of cerebral embolism.

John Jacob Kirschenmann ● Brooklyn; Long Island College Hospital, Brooklyn, 1924; on the staff of the Norwegian Lutheran Deaconess Home and Hospital; aged 40; died, October 5, in Phoenix, Ariz., of tuberculosis of the lungs.

Carlyle Walter Dewey, Conneaut, Ohio; Cleveland Homeopathic Medical College, 1910; city health officer; member of the state medical board; formerly county coroner and member of the board of education; aged 58; died, October 22.

William Walter Wyatt, Peoria, Ill.; Illinois Medical College, Chicago, 1903; member of the Illinois State Medical Society; served the Methodist Hospital in various capacities; aged 74; died, October 22, of coronary thrombosis.

Willis Dowd Gilmore ● Phoenix, Ariz.; University of North Carolina School of Medicine, 1903; tuberculosis consultant for the state board of health; aged 61; died, October 19, in Ann Arbor, Mich., of heart disease.

Frederick Philip Mann ● Valley Falls, Kan.; St. Louis University School of Medicine, 1904; served during the World War; on the staff of St. Francis Hospital, Topeka; aged 61; died, October 16, of cerebral hemorrhage.

James M. Erwin, Calhoun, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1898; member of the Medical Association of Georgia; aged 75; died, October 19, of injuries received when struck by an automobile.

Albert J. Howell, Bay Port, Mich.; Detroit College of Medicine, 1896; member of the Michigan State Medical Society; aged 70; died, October 7, in the Hubbard Memorial Hospital, Bad Axe, of angina pectoris.

Arthur P. Shearburn, Walnut, Ill.; Chicago Homeopathic Medical College, 1893; member of the school board and formerly mayor; aged 77; died, October 8, in the Julia Rackley Perry Memorial Hospital, Princeton.

Franklin Fletcher Dunham, Winnipeg, Man., Canada; Manitoba Medical College, Winnipeg, 1913; aged 52; died, October 31, at the Deer Lodge (Man.) Hospital of coronary thrombosis and chronic pericarditis.

Francis Marion Sanders, Herrin, Ill.; St. Louis College of Physicians and Surgeons, 1904; member of the Illinois State Medical Society; was a member of the school board; aged 72; died, October 19, of heart disease.

James Wilson Cowart, Walden, Ga.; Tulane University of Louisiana School of Medicine, New Orleans, 1894; member of the Medical Association of Georgia; aged 69; died, October 11, of aplastic anemia.

Perry Oliver Englerth, North Judson, Ind.; Kentucky School of Medicine, Louisville, 1896; member of the Indiana State Medical Association; aged 65; died, October 25, of coronary thrombosis.

Adolph O. Speckhard, Bay City, Mich.; Fort Wayne College of Medicine, 1896; member of the Michigan State Medical Society; aged 75; died, October 19, of benign hypertrophy of the prostate.

William Orlando Durham, Maxeys, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1893; aged 70; died, October 5, of cerebral thrombosis, arteriosclerosis and hypertension.

Johanna Baptistella Leo, New York; Woman's Medical College of Pennsylvania, Philadelphia, 1897; member of the Medical Society of the State of New York; aged 75; died, October 20.

William F. Cleveland, Evansville, Ind.; Kentucky School of Medicine, Louisville, 1892; member of the Indiana State Medical Association; formerly state senator; aged 83; died, October 10.

Harry Alonzo Lewis, Continental, Ohio; Toledo Medical College, 1896; member of the Ohio State Medical Association; formerly mayor; aged 80; died, October 7, of coronary thrombosis.

Robert Brown ● San Francisco; College of Physicians and Surgeons of San Francisco, 1911; aged 61; died, September 13, in St. Francis Hospital of coronary occlusion and arteriosclerosis.

William Stanley Reilly, Joliet, Ill.; St. Louis University School of Medicine, 1917; served during the World War; aged 47; died, September 26, in the Veterans Administration Facility, Hines.

Charles T. Granger, Rochester, Minn.; Hahnemann Medical College and Hospital, Chicago, 1892; aged 69; died, October 4, of cardiac decompensation, arteriosclerosis and bronchopneumonia.

Anton Philip Freund, Chicago; Bennett Medical College, Chicago, 1911; served in the U. S. Public Health Service; on the staff of the American Hospital; aged 76; died, October 15.

Guy Watts Wagner ● Chicago; Northwestern University Medical School, Chicago, 1899; served during the World War; on the staff of the Henrotin Hospital; aged 65; died, October 7.

Philip Berry Thomas, Decatur, Ind.; Chicago Medical College, 1885; for many years secretary of the city board of health; aged 79; died, September 20, of cerebral hemorrhage.

Arthur Miller Northrup, Wilkes-Barre, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; aged 61; died, October 3, in the Pembroke (Ont.) Hospital.

Harry J. Phillips ● Louisville, Ky.; University of Louisville Medical Department, 1893; aged 67; died, October 10, in the Kentucky Baptist Hospital of a streptococcic infection.

Oliver P. Morton Ford ● Centerville, Ind.; Medical College of Ohio, Cincinnati, 1889; aged 75; died, October 25, in the Reid Memorial Hospital, Richmond, of heart disease.

Louis I. Melnick, Los Angeles; University of Vermont College of Medicine, Burlington, 1919; aged 53; died, September 12, of coronary occlusion and chronic myocarditis.

Frances Pearl Frank Zumwalt, Tulare, Calif.; College of Physicians and Surgeons, Los Angeles, 1917; aged 45; died, September 13, of metastatic carcinomatosis.

Clarence Gilliam Reno, Summit, Ky.; University of Louisville (Ky.) Medical Department, 1897; served during the World War; aged 66; died, October 5.

William Duff Forrest, Halifax, N. S., Canada; Halifax Medical College, 1898; L.R.C.P., London, and M.R.C.S., England, 1901; died, September 12.

Wyllis A. Silliman, Alameda, Calif.; University of the City of New York Medical Department, 1886; aged 81; died recently of asphyxiation due to submersion.

Charles Edward Jeffery, Lincoln, Mich.; Trinity Medical College, Toronto, Ont., Canada, 1895; aged 68; died, October 18, in Woodbridge, Ont., Canada.

Drury Leigh Fish, Phoenix, Ariz.; St. Louis University School of Medicine, 1909; aged 53; died, October 8, of myocarditis and intestinal obstruction.

Frank L. Herman, Conover, N. C.; Louisville (Ky.) Medical College, 1892; aged 79; died, October 28, of coronary thrombosis and arteriosclerosis.

Frank Russell Morgan, Los Angeles; Hahnemann Medical College and Hospital, Chicago, 1905; aged 60; died, September 13, of angina pectoris.

Fred Buxton Larimore, New Philadelphia, Ohio; Starling Medical College, Columbus, 1903; aged 61; died, October 15, of pulmonary tuberculosis.

Aaron Bockar, Brooklyn; Illinois Medical College, Chicago, 1899; aged 65; died, September 28, in the Crown Heights Hospital of hemiplegia.

Lionel John Samuel Sicard, Buckingham, Que., Canada; McGill University Faculty of Medicine, Montreal, 1919; aged 44; died, September 21.

Frank Galbraith Leslie, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1899; aged 65; was shot and killed, September 15.

John Francis Macaulay, Castalia, N. B., Canada; McGill University Faculty of Medicine, Montreal, Que., 1898; aged 62; died, September 17.

Edward Francis McCormack, Flushing, N. Y.; Albany Medical College, 1897; died, August 30, of bronchopneumonia and arteriosclerosis.

Allie Hunter Stowe, Pacolet, S. C.; North Carolina Medical College, Charlotte, 1912; aged 58; died, September 10, of coronary occlusion.

John A. Ritter, West Baden Springs, Ind.; University of Louisville (Ky.) Medical Department, 1874; died, October 19, of paraplegia.

Bernard Oliver Amberson ● Chicago; Rush Medical College, Chicago, 1929; aged 37; died, October 18, at Manteno, Ill.

William M. Moore, Pine Bluff, Ark.; Meharry Medical College, Nashville, Tenn., 1905; aged 56; died, September 15.

W. K. Burnett, Winston, Ga.; Chattanooga (Tenn.) Medical College, 1894; aged 70; died, September 19, of myocarditis.

Henry M. Mugg, Clarks Hill, Ind.; Medical College of Indiana, Indianapolis, 1902; aged 64; died, September 17.

Frank Rudolph Coursey, Boston; Tufts College Medical School, Boston, 1912; aged 52; died, September 11.

Bureau of Investigation

MISBRANDED "PATENT MEDICINES"

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE.—The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the composition; (4) the type of nostrum; (5) the reason for the charge of misbranding, and (6) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

Cannon's Salve.—Dr. J. Cannon Salve Co., Ltd., Petoskey, Mich. Composition: Essentially a lead compound in a fatty base. For frozen feet, eczema, mad dog bite, blood poison, boils, etc. Fraudulent therapeutic claims.—[*N. J. 29774; March 1939.*]

Dodd's New Discovery.—Stotts Medicine Co., West Memphis, Ark. Composition: Essentially water, sugar, alcohol, chloroform, oil of sassafras and menthol. Fraudulently represented as a cure for pneumonia, asthma, tuberculosis, and other lung and bronchial troubles.—[*N. J. 29771; March 1939.*]

Hauser Potassium Broth.—Modern Health Products, Inc., Milwaukee. Composition: Essentially ground dried plant materials including pea, carrot, onion, celery and alfalfa, with common salt. Misbranded because played up as a health product and because falsely represented to be a potassium preparation and a highly concentrated alkaline broth. Fraudulent therapeutic claims.—[*N. J. 29765; March 1939.*]

[An earlier Notice of Judgment (26484, May 1937) charging similarly fraudulent claims made for this and the two foregoing products was the subject of an extended article in the Bureau of Investigation Department of THE JOURNAL, June 19, 1937, p. 2155.]

Lal Tablets No. 2.—Lal Pharmacal Co., New York. Composition: Essentially acetophenetidin (about 2 grains per tablet), aspirin and caffeine. Misbranded because presence and amount of acetophenetidin were not declared and because the product was fraudulently represented as a remedy for la grippe.—[*N. J. 29754; March 1939.*]

Norwesco Rub.—McKesson & Robbins, Blumauer-Frank Division, Portland, Ore. Composition: A grease containing oil of eucalyptus. Fraudulently represented as efficacious in surface inflammations, croup, coughs, deep chest colds and incipient pneumonia.—[*N. J. 29762; March 1939.*]

Millerlene.—J. S. Miller, Inc., New Jersey (town not given). Composition: Essentially ground senna leaves with small amounts of other plant material, including possibly buckthorn bark and gentian root. Fraudulently represented as virtually a cure-all.—[*N. J. 29787; March 1939.*]

Parlagen Tablets.—American Drug & Chemical Co., Minneapolis. Composition: Rochelle salt, starch and a small amount of a chlorine-liberating compound. Fraudulently represented as having antiseptic and germicidal action in "feminine hygiene."—[*N. J. 29763; March 1939.*]

[San-Tox] Nurse Brand Blackberry Root and Ginger Compound.—De Pree Co., Holland, Mich. Composition: Essentially extracts of plant material (including ginger), and a small amount of volatile oils (including cloves and nutmeg) with alcohol and water. Fraudulently represented as a cure for relaxed conditions of the bowels.—[*N. J. 29793; March 1939.*]

[San-Tox] Nurse Brand Boil Salve.—De Pree Co., Holland, Mich. Composition: Essentially zinc oxide and a small amount of carbolic acid in a specially prepared base. Fraudulently represented as effective in aborting incipient boils.—[*N. J. 29791; March 1939.*]

San-Tox Nurse Brand Flaxseed.—De Pree Co., Holland, Mich. Composition: Ordinary flaxseed. Fraudulently represented as a relief for habitual constipation and a cure for catarrh, dysentery and other inflammatory disorders of mucous membranes of lungs, intestines and urinary tract.—[*N. J. 29795; March 1939.*]

San-Tox Nurse Ground Catnip Herb.—De Pree Co., Holland, Mich. Composition: Common catnip. Fraudulently represented as a cure for colic in children and as an emmenagogue.—[*N. J. 29791; March 1939.*]

San-Tox Nurse Brand Pennyroyal.—De Pree Co., Holland, Mich. Composition: Chiefly leaf fragments, seeds and seed pods of pennyroyal, contaminated with a large amount of rodent excreta. Adulterated because not composed of dried leaves and flowering tops of pennyroyal and misbranded because the term "Pennyroyal" was false and misleading.—[*N. J. 29793; March 1939.*]

San-Tox Nurse Brand Sage Leaves.—De Pree Co., Holland, Mich. Composition: Common sage leaves. Fraudulently represented as a tonic and as an aid in the treatment of malaria, excessive sweats and rheumatic fevers.—[*N. J. 29781; March 1939.*]

[San-Tox] Nurse Brand Sarsaparilla Compound.—De Pree Co., Holland, Mich. Composition: Essentially potassium iodide, extracts of plant drugs (including a laxative), alcohol, sugar and water. Fraudulently represented as a blood purifier.—[*N. J. 29791; March 1939.*]

San-Tox Stomach Bitters.—De Pree Co., Holland, Mich. Composition: Essentially extracts of plant drugs (including an alkaloid-bearing drug), sugar and water. Fraudulently represented to increase the number of white blood cells, correct loss of appetite, incomplete digestion, dyspepsia, etc.—[*N. J. 29793; March 1939.*]

Soap Lake Salts.—Soap Lake Products Corp., Seattle. Composition: Essentially common salt, washing soda, Glauber's salt and a small amount of potassium chloride. Representations as to its efficacy in treating rheumatism, eczema, pyorrhea, gangrene, etc., were declared fraudulent.—[*N. J. 29755; March 1939.*]

Vitatonic.—Edward Hidden, New York. Composition: Essentially extracts of plant drugs including nux vomica and a laxative drug, alcohol (14.4 per cent by volume) and water. Fraudulently represented as a "body builder" and a remedy for kidney, liver and stomach disorders.—[*N. J. 29764; March 1939.*]

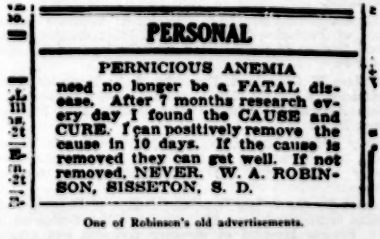
ROBINSON'S PERNICIOUS ANEMIA CURE

The Mails Are Closed to a Dangerous Fraud

More than fourteen years ago the Bureau of Investigation looked into a dangerous fake exploited by one W. A. Robinson, of Sisseton, S. D. Following the investigation the facts were given to the medical profession and the public through an article published in this department of THE JOURNAL and later reproduced in a condensed form in "Nostrums and Quackery and Pseudo-Medicine," Volume III, published by the American Medical Association. The condensed report from the book follows:

Robinson's Pernicious Anemia Cure.—From Sisseton, S. D., one W. A. Robinson exploited an alleged cure for pernicious anemia. Original letters written by Robinson indicated that he was a man without any general education and was obviously ignorant of medicine. Robinson's story was to the effect that in 1919 he had what the physicians had diagnosed as pernicious anemia and was told that it was unlikely that he would get well. He then set about it to find a cure for his condition and this he claimed to have done. Robinson's theory of the etiology of pernicious anemia was not new; it was to the effect that the condition is caused by intestinal parasites. He called these parasites "Anemias" and declared that pernicious anemia "is not a disease at all, any more than 'cooties' is a disease." Robinson claimed that he kept up his "research" on the cause and cure of pernicious anemia for nearly seven months (!) and then found both the cause and the cure; that he cured himself and two friends before he began putting the thing on the market. Robinson charged $30 for his treatment, which he claimed would entirely remove the cause of pernicious anemia in twenty-five days. The treatment consisted of two parts; one was coarse, sharp sand and the other was sometimes a green colored liquid and sometimes some "liver pills." One patient suffering from pernicious anemia took Robinson's nostrum and the sand caused hemorrhages, resulting in the patient's death. Another victim also died following the use of Robinson's treatment and his physician wrote that the end was hastened by the gastric disturbances induced by the treatment.—*(Condensed from The Journal A. M. A., Oct. 24, 1925.)*

The original article was published in THE JOURNAL Oct. 24, 1925. In 1928 the Post Office Department called on Robinson to show cause why a fraud order should not be issued against


PERSONAL

PERNICIOUS ANEMIA

need no longer be a FATAL disease. After 7 months research every day I found the CAUSE and CURE. I can positively remove the cause in 10 days. If the cause is removed they can get well. If not removed, NEVER. W. A. ROBINSON, SISSETON, S. D.

One of Robinson's old advertisements.

him. In order to escape having the mails closed to him, Robinson on June 14, 1928, executed and filed with the Post Office Department in Washington an affidavit in which he swore that he had "absolutely discontinued" his business of selling an alleged cure for pernicious anemia and he promised that the business would "not be resumed at any time in the future."

But in 1936 Robinson was again advertising his "cure." The Post Office Department once more intervened and finally on March 22, 1939, a fraud order was issued against W. A. Robinson, of Sisseton, S. D., closing the mails both to the fraud and to the quack who had conducted it.

Correspondence

INTESTINAL OBSTRUCTION AFTER COLLOIDAL ALUMINUM HYDROXIDE

To the Editor:—In THE JOURNAL October 21, page 1564, appears the report of a case of intestinal obstruction supposedly caused by colloidal aluminum hydroxide. There is much additional information to be desired to that contained in this report. First, what was the diet of the patient while she was receiving the continuous intragastric drip of aluminum hydroxide? From the author's description the material found to be obstructing the small bowel would seem as likely to have been composed of milk curds as anything else. If the patient was largely on a milk diet and the milk was unmodified by the addition of lactose and sodium citrate the formation of curds could be expected. Secondly, if it was to be proved that the aluminum hydroxide caused the obstruction why not present a chemical analysis of the obstructing material? These are two points which need further elucidation by the author.

It has been my practice in a not inconsiderable number of cases of ulcer, with and without hemorrhage, to use a more dilute solution of aluminum hydroxide, mixing three parts of water with one part of the drug and giving it at the rate of 1,500 cc. every twenty-four hours, at the same time allowing a rather liberal soft diet.

The constipating effect of aluminum hydroxide has not been shrouded, as the author contends. In sixty-seven recorded cases and many unrecorded cases in which I have used this preparation I have yet to see constipation develop which is not readily alleviated by the proper use of liquid petrolatum.

CLEMENT R. JONES JR., M.D., Pittsburgh.

To the Editor:—The report by Dr. W. Paul Havens, in THE JOURNAL October 21, page 1564, of an alleged case of intestinal obstruction caused by colloidal aluminum hydroxide deserves some comment, since the use of this antacid either by mouth or by intragastric drip has become quite extensive.

In the case reported, sickness followed severe hemorrhage and 8 cc. of colloidal aluminum hydroxide was administered every two hours for three and a half days, followed by the constant drip of 2,000 cc. of a 1:2 dilution every twenty-four hours. Liquid petrolatum was used only once, but morphine sulfate 10 mg. was administered every four hours for several days. The specific effect of morphine is to contract sphincters, in this way producing a marked degree of constipation.

The evidence of an actual obstruction of the bowel, however, is not convincing. There was no vomiting and apparently only a moderate degree of gaseous distention of the bowel proximal to the lower third of the ileum. The rectum was reported to be full at autopsy after effective enemas. Obviously the intestinal contents were moving downward. It is a question whether the same conditions would not have been found at autopsy in any case in which morphine had been given over a period of days after the ingestion of any other material including bulky food residue.

An opiate should not be used in connection with the aluminum hydroxide drip treatment except in the occasional case in which there is an atypical reaction of diarrhea. For all others, phenobarbital and novatropine or other sedatives are used liberally and liquid petrolatum in one-half ounce (15 cc.) quantities two or three times a day. With these precautions in a series of 407 cases (101 presenting massive hemorrhage) there has been no instance of intestinal obstruction. In the earlier cases there were many instances of an accidental inflow of a whole flask of the aluminum suspension in a short time owing to an air leak in the siphonage system. There usually was no disturbance of the bowel and never as much difficulty in the elimination of this excess as in some cases of barium retention after x-ray examination. In some cases there will be firm scybala palpable in the left iliac fossa, but with a more liberal use of liquid petrolatum by mouth, an occasional oil enema and the avoidance of opiates impactions are prevented.

If one is familiar with the mildly constipating character of aluminum hydroxide and takes the necessary precautions, especially with the drip treatment, there should be no serious difficulty with the matter of constipation or danger of true mechanical obstruction of the bowel. The astringent properties of aluminum hydroxide seem to have certain advantages in the treatment of ulcer, and many patients testify that symptomatic relief is more complete than with magnesium trisilicate, which is sometimes substituted. The combination of the two nonalkalizing antacids is often useful in ambulatory management.

If the whole principle of antacid therapy is sound, certainly the principle of continuous night and day neutralization is sound. X-ray and other evidence indicates that healing may be obtained in as short a period as ten days and in a higher percentage of cases than can be obtained by the older medical managements over a period of three weeks or more. Hence the importance of getting the exact facts about minor difficulties and the technic to avoid them.

V. C. ROWLAND, M.D.
E. E. WOLDMAN, M.D.
Cleveland.

"EXPERIMENTAL CHEMOTHERAPY WITH SULFANILAMIDE AND RELATED COMPOUNDS"

[An addendum to paper in THE JOURNAL November 4]

To the Editor:—An exception to the specificity of the reaction for the detection of oxidation products of aromatic amines (described in *Public Health Reports* 54:1880 [Oct. 20] 1939) has been found in that positive results were obtained with the glucosides of sulfanilamide and 4,4'-diaminodiphenyl sulfone. Apparently this linkage protects the amino group from acetylation, but the glucoside is later split off by the nitrous acid employed in diazotization.

Observations made with the original technic must be interpreted in the light of these observations. Our results on urinary excretion of a hydroxylamine derivative following administration of sulfanilamide must be reexamined to determine to what extent other derivatives were involved in the reaction.

Attempts are being made to modify the procedure so that these difficulties will be overcome.

SANFORD M. ROSENTHAL, M.D., Washington, D. C.
Senior Pharmacologist, U. S. Public Health Service.

ELECTROCARDIOGRAMS

To the Editor:—In the August 12 issue of THE JOURNAL, Drs. Strouse, Katz and Binswanger discussed a feature of electrocardiographic study which is worthy of reemphasis. Textbooks and the literature have not sufficiently stressed the problem and the significance of basic and serial electrocardiograms. By careful study of patients and graphs one finds that the single picture is usually of no clinical value except as it presents definite diagnostic features. Especially is this true in coronary disease on an arteriosclerotic basis, in which progression of the pathologic condition may take place without clinical exhibition of variation in cardiac disorders or even in symptomatology.

It seems that the best way to detect lesions early is by taking the patient's cardiac "fingerprints" and follow these up subsequently; i. e., a routine electrocardiogram of all patients over the age of 40 at the time of a general physical examination. Later follow-ups will help in early diagnosis of the presence or extension of disease by comparative study. It is in coronary

disease that this procedure will have inestimable value and possibly help in preventing early or avoidable cardiac morbidity.

Here is an example of the importance of an early presymptomatic electrocardiogram. It is known that the T wave may be normally inverted in lead 3. But it is not known what the normal is for any individual unless one has his cardiac "fingerprints." A man of 62 with no symptoms had a normal electrocardiogram in the four leads with inverted T_3, which is not considered pathologic. Four months later the first manifestation of posterior infarction was pain in the back, but the electrocardiogram showed an erect T_3, which had been inverted. This was interpreted as a coronary disorder and within two days a typical graph of occlusion was evident. If the "normal" electrocardiogram had not been available, a case of this sort might have been overlooked.

The electrocardiogram, when properly used and interpreted, is an extremely useful adjunct to the history and examination in arriving at a definite diagnosis and prognosis in some cases in which doubt would prevail regarding the management of the case.

Since heart disease has assumed the position of Osler's "Captain of the Men of Death," I feel that this plea for early and serial electrocardiograms should seriously be considered by all doing cardiac work.

SAMUEL WALDMAN, M.D., Brooklyn.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ANGINA PECTORIS, NEUROCIRCULATORY ASTHENIA AND MENOPAUSE

To the Editor:—Two years ago a married Jewish woman 31 years old developed an anginal syndrome parallel with her menopausal syndrome. Only since two months ago has definite evidence of coronary sclerosis been identified by electrocardiograph. She has never had decompensation, but lately some cyanosis of the lips and finger nails has been visible and paroxysmal tachycardia has developed. Since the prognosis is apparently poor and since it is felt that her years are numbered, I wish you could tell me whether the injection of alcohol into the sympathetic and parasympathetic ganglions and nerves of those leading to the heart is rational therapy and what neurosurgeons are capable of performing these injections. Glyceryl trinitrate and other vasodilators have been used without success. What other types of therapy may safely be used on this form of heart disease? Jacob C. Dorfman, M.D., Rochester, N.Y.

ANSWER.—It is most important in the first place to be absolutely certain of the diagnosis of angina pectoris in this patient with the menopause. She is probably in a highly nervous state and one must carefully rule out neurocirculatory asthenia, which will be associated frequently with heartache and anterior chest pain. The very failure of her discomfort to be relieved by glyceryl trinitrate is strong evidence against angina pectoris.

The electrocardiographic evidence of coronary disease does not prove the presence of angina pectoris. She might have either one alone, and many persons with neurocirculatory asthenia have also electrocardiographic evidence of coronary disease without any angina pectoris. There are in this case some evidences of irritability of the heart and circulation not necessarily in keeping with coronary disease, for example cyanosis of the lips and finger nails and paroxysmal tachycardia.

If, however, the most careful consideration indicates the presence of an important and, to a certain extent, a crippling degree of real angina pectoris, radical therapy should be considered. However, it is best to try to postpone it until after the menopause is completed because the clearing of the menopause itself may result in definite improvement and moreover there are many instances of spontaneous recovery from coronary insufficiency. This has been found to be almost the rule. Coronary disease may continue, of course, but the development of collateral coronary circulation renders the state of health much better.

Paravertebral injection of alcohol is, although helpful, to be considered a radical measure and to be postponed until all adequate medical measures, including nitrites, have proved unavailing. It is well to wait a year or two or more before undertaking any radical methods of treatment unless the situation is really bad.

MYOTONIA ACQUISITA

To the Editor:—A patient for whom I have made a diagnosis of myotonia acquisita rather than myotonia congenita shows generalized rigidity with a tendency to corrugation of muscles when they are stimulated. He shows no symptoms which would lead to the diagnosis of tetany. In line with the recommendations in the literature, he has been receiving quinine sulfate by mouth, beginning at 15 grains (1 Gm.) daily and increasing to as high as 30 grains daily. He has also received calcium intravenously, and on several occasions he stated that he "loosened up" for some time after the injection. However, now he does not seem to have a favorable response from the treatment I am giving him. Can you suggest any other form of therapy which might prove helpful?

George B. Fletcher, M.D., Hot Springs National Park, Ark.

ANSWER.—Not enough of the patient's symptoms are given for one to be sure that the diagnosis of myotonia acquisita is correct. One would want to know the patient's age, his previous history with regard to neuritis and whether the condition was familial or hereditary. One fact, however, probably points to a diagnosis of myotonia acquisita. The patient has been receiving quinine in adequate dosage without favorable response. This in itself indicates that the disease is of the acquired type rather than myotonia congenita. Alexander Wolf (An Effective Form of Treatment for Myotonia, *Arch. Neurol. & Psychiat.* 36:382 [Aug.] 1936) and other investigators have shown conclusively, and it has been observed by others, that patients with myotonia congenita respond quickly to quinine. It is possible, therefore, that the lack of response by this patient is helpful in making the diagnosis. A favorable response to quinine is not to be expected in the acquired form of myotonia.

It is felt by most investigators at the present time that myotonia acquisita is not a familial or hereditary disease. It may follow neuritis of a mild type, and the hypertrophy of the muscles found in this condition is indistinguishable from that found after neuritis. The condition usually occurs in early adult life, often is mild and may go on to complete recovery. The disease is rare and only a few cases have been reported in the literature. Myotonia congenita, however, is more common, although it too is rare. If there is any evidence of neuritis, such as tenderness along the course of the nerves, lost reflexes, vasomotor or trophic changes, or alterations in the electrical responses, treatment should be directed toward the neuritis itself.

Any specific treatment for myotonia acquisita is not known. Knud H. Krabbe (Myotonia Acquisita in Relation to Postneuritic Muscular Hypertrophies, *Brain* 57:184 [June] 1934) simply stated that his patient "was given thyroid extract and improved considerably; power and rate of movement increased and the muscles seemed to diminish in bulk." If, as Krabbe suggests, the condition is due to "excessive" recovery from the polyneuritis, thiamin chloride appears not to be indicated. The response in patients with the atrophic form of myotonia to amphetamine sulfate is encouraging. From 5 to 20 mg. a day may be given, in two or four doses. Although no reports of its use in myotonia acquisita are at hand, it is worthy of trial. It must not be forgotten, however, that spontaneous recovery from myotonia acquisita is not unknown. Sources of infection in the body which might give rise to polyneuritis are to be sought for. Mild gymnastics are advocated and a warm climate is said to be beneficial.

FETOR ORIS

To the Editor:—Please discuss causes, physical and chemical, of fetor oris arising from the oral cavity. M.D., Massachusetts.

ANSWER.—Fetor oris originating in the oral cavity may be divided into three types, arising from (1) retained food particles or their decomposition products, (2) decomposition of oral tissues or fluids and (3) volatile substances absorbed elsewhere in the body and released from oral tissues or fluids secreted into the oral cavity. By the use of a method described by Brening, Sulser and Fosdick it is possible to gain some idea of both the intensity of the odors and their source with respect to the part played by the lungs, nasal cavity and oral cavity.

There appears to be disagreement among investigators with respect to the importance of the role which food particles play. Some believe that they are relatively insignificant; others offer evidence that such substances as onion and garlic chewed but not swallowed may be detected from sixty to seventy-two hours after mastication. The period is appreciably longer than when

the same substances are ingested by capsule. The physical opportunities for lodgment and decomposition of food débris offered by the embrasures between the teeth, cavities produced by caries or other mechanical places of advantage appear to be generally recognized factors. Oral chemical reactions occurring in degenerative and suppurative lesions in the mouth such as pyorrhea are unquestionably of importance. Some believe that the stagnation of oral fluids and desquamation of epithelium of the mucosa may give rise to unpleasant odors. The lesions of dental caries affecting only the calcified tissues of the teeth are less significant, but the opportunities which they offer for the lodgment of food allow putrefactive changes, and their extension to the point of exposure of the dental pulp may initiate degenerative changes in that organ which can unquestionably contribute to fetor oris.

In addition to these regional causes there is considerable evidence indicating that the oral secretions may give up volatile substances which were assimilated by the blood and other tissue fluids from the gastrointestinal tract, the lungs or other organs. The existence of this systemic factor has been proved experimentally but its relative importance when evaluated with respect to the regional factors is still debatable. All must be carefully investigated when searching a cause in a specific instance.

The following references together with their bibliographies may prove of value to any one interested in pursuing the subject:

Brening, R. H.; Sulser, Glenn F., and Fosdick, Leonard S.: The Determination of Halitosis by Use of the Osmoscope and the Cryoscopic Method, *J. Dent. Research* **18**:127 (April) 1939.

Sulser, Glenn F.; Brening, R. H., and Fosdick, Leonard S.: Some Conditions That Affect the Odor Concentration of Breath, *J. Dent. Research* **18**:355 (Aug.) 1939.

POSITIONAL CHANGE OF FETUS IN UTERO

To the *Editor*:—Can you give me some idea as to what might be found in the literature concerning change of position and presentation of the fetus during the last month of pregnancy? On two occasions in the antepartum clinic I have seen the diagnosis of the presentation reversed at delivery within a week of the last examination. When I talked to several physicians concerning this, opinion was varied. Most had had a similar experience, but many felt that they had been incorrect in their original diagnosis. A few were certain that their diagnosis had been correct and that the fetus had changed position. On Aug. 3, 1939, in our antepartum clinic we examined for the first time a 44 year old primigravida. In the attempt to ascertain the position of the fetus, neither the external nor the pelvic examination was entirely satisfactory. This was due to the fact that the patient was large and obese (230 pounds [113 Kg.]). Further examination disclosed a blood pressure of 180 systolic and 110 diastolic, edematous ankles and moderate anemia. A roentgenogram taken at this time showed the fetus in a transverse position with the head to the right. The fetus appeared to be near full term and according to the menstrual history delivery was due about August 25. We decided it would be best to hospitalize the patient, attempt to control her pre-eclampsia, build up her blood and seek consultation as to the feasibility of performing a cesarean section. The consultant advised complete bed rest, restricted fluids, salt-free diet, iron and liver and an x-ray check-up in a week. After one week of this regimen the ankle edema disappeared, the blood pressure went down to 150/90, and the red count and hemoglobin improved. The roentgenogram taken at this time (August 11) showed a breech presentation with the sacrum to the right. In view of this observation it was decided to make pelvimetric determinations by means of roentgen precision stereoscopy. The next day (August 12) this showed a vertex presentation, with the occiput to the right anteriorly. There was no disproportion. On September 6 the patient went into labor and a roentgenogram taken at this time showed the presentation to be vertex with the occiput to the left. The patient was delivered of a living boy with low forceps.

This series of roentgenograms, particularly the two taken in twenty-four hours which showed a change from breech to vertex presentation, was especially interesting, more so because this had taken place while the patient was at complete bed rest and there had been no attempted external manipulation. Can you tell me whether or not a change in presentation of a fetus over a twenty-four hour period is recognized as a fairly common occurrence and whether there has been any work done in this line and verified by x-rays?

Nicholas P. Dallis, M.D., Glen Cove, N.Y.

ANSWER. — Presentation and position are the result of a process of accommodation of the fetus to the uterus and the pelvis. Many factors may influence normal accommodation in utero during the last part of pregnancy and result in varying presentations and positions. An excessive amount of liquor amnii, relaxation of the abdominal wall, an unusually large pelvis, abnormalities of the fetus and abnormalities of the uterus are some of these factors.

Normally when the presenting part becomes engaged in the inlet of the pelvis no change in presentation can occur. In the primipara engagement usually takes place during the last month of the pregnancy. However, when this does not occur a change of polarity and of position of the presenting part can easily take place. During the seventh and eighth months of gestation many babies present by the breech. These breech presentations most often change into cephalic before engagement takes place. Many observers have noted a change in polarity within a period of hours or days.

The patient in question undoubtedly had a large pelvis, which may have been a factor in the change in polarity and position of the fetus. Undoubtedly, such changes in presentation and position occur commonly without the knowledge of physicians. No report of careful study of this problem by means of frequent roentgenograms has been found.

EOSINOPHILS IN RHINITIS—DEGREE OF SUFFERING IN HAY FEVER

To the *Editor*:—1. In a case of rhinitis of questionable etiology does the presence or absence of large numbers of eosinophils in the nasal secretions indicate or exclude hypersensitiveness as the cause? 2. Two patients have received prophylactic treatment by the parenteral method for dwarf and giant ragweed hay fever for the past three years. Prior to the onset of the fall hay fever season both received up to 10,000 pollen units of mixed extract. They were remarkably free of symptoms during the first two years but have suffered rather severely during the present season. Intervals of injection and dosage have been identical each year. What can be the explanation for this phenomenon?

M.D., New York.

ANSWER.—1. The presence of a large number of eosinophils in the nasal smear is definite proof that the rhinitis is of an allergic nature. If only a few eosinophils are present the diagnosis becomes somewhat doubtful and must then be deduced from the history, the presence of some other allergic conditions in the patient or of allergy in the family and from cutaneous tests. The absence of eosinophils does not exclude allergy. If a patient with allergic rhinitis develops an ordinary infectious coryza, the nasal smear will usually show a temporary diminution or absence of eosinophils and a predominance of polymorphonuclear cells.

2. There are four possible explanations for the increased suffering. First, the ragweed hay fever season this year, in certain parts of the country, at least, has been much more severe than in any previous year since 1935. For example, in the Middle West the amount of ragweed pollen has been from 50 to 75 per cent greater than in 1938. Second, the material used for injections may not have been up to standard; perhaps it had deteriorated. New extracts should be used every year and some physicians prefer to change their solutions every few months. Third, the two patients may possibly belong to the small group whose symptoms seem to become aggravated more and more as they receive injections. Fortunately, the large majority seem to improve year after year under treatment. Fourth, some physicians believe that pollen varies in toxicity from year to year. This is difficult to prove, but from the large amount of hay fever suffering this season, it might well be a factor.

HERRMANN MEASUREMENTS OF HEART AND MALINER'S TEST

To the *Editor*:—Will you please evaluate, explain and give me some information on (1) Herrmann measurements of the heart and (2) Maliner's test. If the Herrmann measurements showed an enlargement of the heart but the cardiothoracic ratio was normal and there was no clinical evidence of any heart condition, would you not believe that the cardiothoracic ratio was probably the correct determination?

M.D., Illinois.

ANSWER.—Herrmann's measurements of the heart consist of comparison of the weight of the left ventricle with the weight of the right ventricle by a special method of dissection different somewhat from that carried out by Lewis, in which the septum was dissected away in toto. Herrmann's method has been described in the *American Heart Journal* (**1**:213 [Dec.] 1925). The ratio which he found in the dog's heart, L/R (ratio of left ventricle to right ventricle), was 1.393 with a minimum of 1.153 and a maximum of 1.773. By Lewis's method this ratio averaged 1.461 with a minimum of 1.450 and a maximum of 1.880.

Maliner's test, as reported by M. M. Maliner and W. F. Matthews (*Arch. Pediat.* **56**:142 [March] 1939), is a modification of Master's two step exercise test. Maliner and Matthews studied a group of 200 children and twenty-five noncardiac clinical patients and came to the conclusion that the measure of exercise tolerance as determined by this two step test is fairly constant but that changes in the pulse rate are less important than variations in the systolic blood pressure. This exercise tolerance test was presented originally by A. M. Master and E. T. Oppenheimer (*Am. J. M. Sc.* **177**:223 [Feb.] 1929) and was further discussed by Master (*Am. Heart J.* **10**:495 [April] 1935).

The roentgenographic cardiothoracic ratio may be normal with no clinical evidence of heart disease and yet the actual size of the heart, especially the ratio of right to left ventricle, may be greater than normal.

SUBACUTE GONORRHEA AND SULFAPYRIDINE

To the Editor:—A man aged 31 had intercourse on August 2 and first noticed a discharge on August 11. He came in for treatment at once and was started on sulfanilamide 60 grains (5 Gm.) daily for five days. The discharge became less for two days and then again became profuse. The dose of sulfanilamide was increased to 120 grains (8 Gm.) daily, and the discharge disappeared in three days. Examination of the prostate and seminal vesicles at that time showed no signs of involvement. A prostatic smear, however, was strongly positive for the gonococcus. The sulfanilamide was reduced to 60 grains daily, and the discharge promptly reappeared. Hand injection with mild protein silver 5 per cent was begun at this time. After a week of this treatment, the sulfanilamide was reduced to 45 grains (3 Gm.) daily. This dosage was maintained until September 6. While there was a decrease in the amount of discharge at that time, there was always some present. With the hope that the organisms would lose their apparent tolerance to the drug, the sulfanilamide was then discontinued for ten days, and irrigations of 1:5,000 acriflavine were given in the office every other day. The hand injections of 5 per cent mild protein silver were continued by the patient at the same time. The sulfanilamide was again given in a dosage of 120 grains daily for three days, then dropped to 60 grains daily. The discharge, while less in quantity, has still persisted and may be obtained at almost any time. The smear is still positive for gonococci, although considerable searching is necessary to find them. It seems to me that this patient has had more than sufficient treatment. Would you suggest that the treatment be continued or changed? What treatment do you believe advisable? What is M. & B. 693, and where can it be obtained? Some of the British literature seems to favor this drug over sulfanilamide.

M.D., Iowa.

ANSWER.—From the history given, this is a case of subacute gonorrhea probably with some involvement of the posterior urethra. Before instituting further treatment it would be advisable to do complete blood counts, including differential, since the large doses of sulfanilamide which have been given are apt to produce anemia or other blood dyscrasias. Complete physical examination is also indicated, with special attention to the peripheral nerves. With negative results from these tests it would be safe to institute therapy with sulfapyridine, which is M. & B. 693 and is sold by several leading drug houses. In this case the dose should be 60 grains (4 Gm.) the first day, 40 grains (2.6 Gm.) the second and third days and 30 grains (2 Gm.) for four more days. Local treatment in the form of hand injections of 5 per cent mild protein silver twice a day should be continued, but no more than 4 cc. should be injected and this after micturition. At the end of a week urethral and prostatic smears should be studied, and appropriate tests of cure such as passage of a sound followed by instillation of 0.33⅓ per cent silver nitrate, ingestion of alcohol and intercourse should be tried. If at any time the gonococcus is rediscovered, another course of sulfapyridine should be given exactly as before. This may be necessary because of the chronicity of the involvement and the previous use of large doses of sulfanilamide, which seems to necessitate a larger total dose of sulfapyridine. The effectiveness of sulfapyridine in gonorrhea is estimated to be from two to three times that of sulfanilamide; however, it is always necessary to administer local treatment with either drug.

EFFECT OF SACCHARIN

To the Editor:—What are the deleterious effects of the prolonged use of saccharin? I have a patient who has been using about 10 grains (0.65 Gm.) a day for several years. Occasionally he shows a questionable reaction for albumin in the urine. The patient also has an arrested case of pulmonary tuberculosis. His diabetes is fairly well controlled by diet and insulin.

V. F. Neumann, M.D., Norwich, Conn.

ANSWER.—Blodgett has reported that a patient of his with glycosuria used from 7 to 8 grains (0.45 to 0.52 Gm.) of saccharin daily for twenty-four years with never a symptom that could be attributed to saccharin. He also described several cases in which patients suffering from obesity and treated with diets restricted in carbohydrate had used saccharin daily for fifteen years without deleterious effect. Blodgett considered saccharin a condiment and not a drug. Wilcox studied the therapeutics of saccharin and concluded that it may be used indefinitely in amounts tolerable to taste without harm. Although Sollmann stated that it is harmless and that from 70 to 90 per cent is excreted unchanged in the urine, cases of saccharin poisoning have been reported by Grundfest and by Heilmann. However, no albuminuria was found and the doses used were enormous. By far the most complete study on the physiologic actions of saccharin was that made by Carlson and his associates for the Referee Board. They found that a dog with 75 per cent of its total kidney tissue removed by nephrectomy could be given from 5 to 20 Gm. of saccharin daily for six weeks without any effect on kidney function or nitrogen metabolism but that intravenous injection of from 10 to 25 Gm. of saccharin into a dog with only one kidney or into a normal dog resulted in some diminution of kidney function as determined by the phenolsulfonphthalein excretion during the first hour. Carlson and his co-workers pointed out that their short term feeding experiments did not exclude the possibility of injurious effects of smaller amounts of saccharin taken over a long period, particularly by persons in the older age groups.

It appears from this evidence that the possibility in the case cited of 0.65 Gm. of saccharin causing albuminuria is remote. While final proof of the matter would require demonstrating that increasing the intake of saccharin caused increased albuminuria and vice versa, the more common causes of traces of albuminuria should be investigated before placing the blame on saccharin.

References:

Blodgett, S. H.: Saccharin, *M. Rec.* **97**: 521 (March 27) 1920.

Carlson, A. J.; Eldridge, C. J.; Martin, H. P., and Foran, F. L.: Studies on the Physiological Action of Saccharin, *J. Metabolic Research* **2**: 451 (March) 1923.

Grundfest, Karl: Ein Fall von Saccharinvergiftung, *Zentralbl. f. inn. Med.* **48**: 234 (March 26) 1921.

Heilmann, Pankraz: Saccharinvergiftung, *München. med. Wchnschr.* **69**: 968 (June 30) 1922.

Sollmann, T. H., and Hanzlik, P. J.: An Introduction to Experimental Pharmacology, Philadelphia, W. B. Saunders Company, 1920, pp. 67-68.

Wilcox, R. W.: The Therapeutics of Benzosulphinide, *M. Rec.* **98**: 595 (Oct. 9) 1920.

ABORTION AND MENSTRUAL FLOW

To the Editor:—A healthy married woman aged 37, mother of two healthy children aged 9 and 5, has the following history: On May 26, 1939, she had her usual normal and regular menstrual period of the twenty-eight day type with four days' duration. On or about June 7 she became pregnant. On July 17 she was hospitalized for spontaneous threatened abortion. On July 22 the abortion was considered inevitable and the uterus was emptied by ovum forceps and curet. On July 29 she was discharged from the hospital after an uneventful postoperative course. On August 5 she was with her husband for the first time after the operation. On August 12 she started bleeding at what she considered the right time had she not become pregnant. After the flow had continued for one month she was regarded by the family physician as functional bleeding, and during the second week of the flow antiuterin-S in the amount of 600 units was given in divided dose. During this second week of flow an occasional stringlike clot was passed but there was no pain. At the beginning of the third week of bleeding progesterone was given on two consecutive days in 1 cubic dram. On the day of the second dose there were cramp pains in the pelvis and back, and a clot the size of a hickory nut was passed but not seen by the physician. On the third day of the third week of flowing the patient was examined by an obstetrician, who said the uterus was slightly enlarged and the os half the size of a finger. He advised a uterine stimulant and in three days the flow stopped and there has been no further flow. 1. How soon after a fruitful coitus might an abortion occur? 2. If this was not an abortion, what might it have been?

M.D., Iowa.

ANSWER.—The involution of the uterus is relatively longer after an early abortion than after a term pregnancy. The woman in question was discharged from the hospital seven days after the uterus was emptied and had intercourse fourteen days after the abortion. Two reasons may be given for the uterine bleeding. Probably the real one is that it was a normal menstrual function, but it might have been from subinvolution of the uterus. Normal menstruation is frequently disturbed for a time following abortions and term pregnancies and usually calls for no treatment. It is difficult to see the reason for the treatment given, certainly as given at that time. Rest in bed, a few hot vaginal douches and ergot would seem to have been more logical. It is common for a multiparous woman to have a slightly enlarged uterus at the period examined. It is possible for an abortion to occur within a few days after a fruitful coitus. The age at which the ovum is embedded in the uterus is not settled but is probably not over eight days. De Lee says that an expelled ovum the size of a pigeon's egg is approximately 4 weeks of age, and one the size of a hen's egg from 6 to 7 weeks.

TUBERCULOUS EMPYEMA AND OLEOTHORAX

To the Editor:—Is there any solution that can be used effectively in cleaning up tuberculous empyema?

M.D., Chicago.

ANSWER.—There is no solution which is effective in cleaning up tuberculous empyema. Oleothorax, however, gives satisfactory results to the extent of from 60 to 70 per cent of the cases in which it is used. To replace the exudate, which is generally removed by aspiration at regular intervals, plain sterilized olive oil without medication is injected into the pleural space. Irrigation with physiologic solution of sodium chloride or with diluted solution of sodium hypochlorite, if preferred, is done with a syringe having a large caliber needle. There is absolute bed rest during the course of treatment.

To guard against any untoward reactions, the first injections of oil are in small amounts, 5, 10 or 20 cc.; then more oil may be added fractionally until the space is filled or the desired indication is reached. In some cases, when the exudate persists, aspirations can be done below the oil level without removing the oil and the amount aspirated replaced with the oil.

V 1
193

This form of treatment has given excellent results in a large number of cases, and no ill effects result from the olive oil. When, however, the pathologic process in the lung beneath the purulent exudate is more advanced, as with secondary infection of the tuberculous empyema, cavitation, bronchopleural fistula or pleurocutaneous fistula, a thoracoplasty may have to be resorted to.

IRREGULAR MENSES AND OBESITY AT MENARCHE

To the Editor:—A girl aged 14 weighing 160 pounds (73 Kg.) is normal to physical examination except for being overweight. Urine and blood tests are normal. Her first menstrual period began Feb. 1, 1939, and was profuse for a week. I gave a preparation of iron to prevent any anemia and stated that menstruation would adjust itself, in all probability. The flow continued, however, and on February 10 her red cell count was 4,980,000. Owing to the general appearance of obesity I gave her thyroid extract, one-half grain (0.03 Gm.) twice a day, and estrogenic-5 every other day for six or eight doses. The flow continued until February 23, at which time a curettage was done. The uterus and genital tract were apparently normal. The laboratory report showed the material from the uterus to be normal. While in the hospital, she was under the care of a gynecologist and was given antianemia-type factor tablets three times a day. Since then she has menstruated fairly regularly two or three times, but now her periods are getting closer together. The last was at an interval of two weeks. Treatment has consisted of thyroid extract, one-half grain twice daily given continuously, and antianemia-type factor, three times a day a week before each menstrual period. Between periods she has had a tiny amount of discharge which has been unrevealing. The parents are rather anxious as to her irregularity. Physically she is in good health. Would progesterone or gonadotropic substance or another of the glandular preparations be beneficial?

M.D., Indiana.

ANSWER.—There is no need to give this child any treatment for her menstrual irregularities at the present time. Undoubtedly the same results would have been obtained without the curettement, which is rarely indicated at puberty. Since the patient is definitely overweight, she should be placed on a diet which will make her lose weight. This may be accomplished without thyroid therapy but in this case the small amounts of thyroid may be helpful. Irregularity of the menses is frequent at onset and may last a year or more. As long as the amount of blood is not excessive and the patient does not become anemic, no special treatment is needed.

CEREBELLAR ATAXIAS

To the Editor:—A patient with cerebellar ataxia has a brother who is worried about also having it because it is hereditary. This brother heard that glandular therapy is preventive treatment. If there is any glandular therapy or other treatment for cerebellar ataxia that is preventive, will you please advise me.

M.D., Illinois.

ANSWER.—There is no known prophylactic (preventive) or active treatment of any of the cerebellar ataxias that are hereditary, familial or both. The ages of the patient and his brother are not mentioned. If the patient is adolescent, he probably has spinal cerebellar ataxia of Friedreich or hereditary cerebellar ataxia of Marie. If he is older (between 30 and 50) he may have the form known as primary progressive cerebellar degeneration of Holmes. All these varieties are due to a defective anlage in the cerebellar structures and there is no treatment.

TRANSMISSIBILITY OF TRACHOMA

To the Editor:—A man aged 54 has had trachoma for ten years. Recently he began supplying a community with raw milk. Should he be allowed to milk, bottle milk or work about the barn or milk house in any capacity?

George S. Enfield, M.D., Bedford, Pa.

ANSWER.—It is necessary to bear in mind that (1) trachoma is not communicable to domestic animals; (2) the infection is disseminated by direct or indirect contact from eye to eye only, never by intestinal or other ports of entry; (3) in general, the dosage for implantation must be repeated or relatively massive; (4) the infectious agent or virus is rapidly inactivated by dilution or when once removed from its normal habitat, and (5) the contagiousness of a given patient decreases with duration of the disease, so that with the possible exception of an acute flare-up a case of ten years' standing would only rarely serve as a source of infection. In this particular instance, therefore, it may be said that, while the idea may offend one's sensibilities and perhaps even oppose more general precepts of public health, the possibility of spreading trachoma under the conditions outlined is extremely remote. Of course pasteurization of milk would eliminate remonstrances from the most conscientious of objectors.

Regarding the matter from the point of view of the patient, it must be remembered that employment about farms, barns and the like maintains a constant exposure to dust, strong variations in light and other factors which promote conditions for exacerbations of trachoma.

MAGNESIUM SULFATE IN CARDIAC ARRHYTHMIAS

To the Editor:—Please outline the rationale for and the technic of the use of magnesium sulfate in paroxysmal tachycardia. In what other forms of heart disease is it indicated?

Allen S. Cotter, M.D., Los Angeles.

ANSWER.—Theoretically and experimentally the magnesium ion is known to depress all muscle and nerve function, and so magnesium sulfate has been suggested for control of disordered heart rhythm, especially premature beats and paroxysmal tachycardia. However, with large enough doses to have such a depressing effect, the toxic action on the myocardium and on the central and peripheral nervous system is of important consideration; experimentally dilatation and standstill of the heart have been produced by magnesium salts. Actually little favorable effect has been found in the use of magnesium in disturbances of heart rhythm. Magnesium sulfate is much more useful in cardiac cases as a mild watery purge in congestive failure. It acts as an osmotic cathartic. Large doses, that is, enough to produce several stools a day, are to be avoided because of the fatigue that ensues. Magnesium is antagonized by calcium.

CORONARY DISEASE AND GOITER

To the Editor:—Is coronary disease more frequent among those who have goiter than among those who do not?

Richard E. Stifel, M.D., Cleveland.

ANSWER.—This is an important question, but a satisfactory answer cannot be given at the present time. What little evidence there is does not support the view that coronary disease is more frequent among those who have goiter. Angina pectoris is rare in patients with toxic goiter and, when it does occur, tends to disappear after a thyroidectomy. In patients with myxedema, angina may first appear during the administration of desiccated thyroid.

THROMBOPLASTIN

To the Editor:—In The Journal, July 29, page 381, is given a test for vitamin K deficiency using thromboplastin with directions for preparing the thromboplastin. Is the ordinary thromboplastin of the drug trade satisfactory? If not, where can the type described be purchased?

M.D., Florida.

ANSWER.—It is believed that none of the preparations of thromboplastin now on the market are suitable for use in the prothrombin test described in the article cited. It should probably be possible to market suitable material in dried form in tubes of a size appropriate for the test. With the directions given in the article mentioned, any one can prepare the material from fresh tissue at relatively slight expense.

NO ELECTRICAL STIMULATION EFFECTIVE FOR PREMATURE EJACULATION

To the Editor:—What apparatus can produce sinusoidal-faradic current of moderate rapidity used in the treatment of ejaculatio precox to tone the weak and relaxed muscles of the penis?

M.D., Philippine Islands.

ANSWER.—No electrical stimulation of muscle will tone weak muscles. With regard to erection of the penis and ejaculation, Wiggers states: "Before coitus can take place the male copulatory organ must become hard and erect. The increased rigidity is due to flooding of the cavernous spaces with blood as a result of dilatation of their afferent arterioles. Compression of external veins by skeletal muscle contraction does not occur. Secondarily, the venous outflow from the efferent veins may be impeded, however, owing to compression from within against the rigid outer coat. Erection, which occurs coincidentally, is not due to muscular action but is produced through a mechanical leverage action of the suspensory ligaments attached to the posterior portion of the cavernous tissue."

CHAULMOOGRA OIL IN TUBERCULOSIS

To the Editor:—I have read with interest your note in the Journal, October 7, page 1432, on chaulmoogra oil in tuberculosis, in which you say "Unfortunately, there is no proof available that chaulmoogra oil has any beneficial effect in the treatment of tuberculosis in any form." I have been interested in this subject and, in going over the references that you cite, notice that one of the most recent reports on this subject is not included. I refer you to an article by Dr. J. Edgar Wallace (*Brit. M. J.* 1:1151 [June 5] 1937) in which he reports encouraging results following the intradermal injection of esters of hydnocarpus oil in lupus vulgaris, as follows: "The intradermal injection of hydnocarpates, in the small number of cases so far available, has produced extremely encouraging results, and appears to offer certain advantages over other routine methods." I am bringing this to your attention because this reference is more recent than any that you cite.

Robert C. Page, M.D., Mount Vernon, N. Y.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, December 2, page 2083.

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 18-20. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ALASKA: Juneau, March 5. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: *Basic Science.* Tucson, Dec. 19. Sec., Dr. Robert L. Nugent, University of Arizona, Tucson. *Medical.* Phoenix, Jan. 2. Sec., Dr. J. H. Patterson, 826 Security Building, Phoenix.

ARKANSAS: *Basic Science.* May or June. Sec., Mr. Louis E. Gehaner, 701 Main St., Little Rock.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, Jan. 17. *Written examination.* Los Angeles, Feb. 26-29. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: *Basic Science.* Denver, Dec. 13-14. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver. *Medical Endorsement.* Denver, Jan. 2. *Medical Examination.* Denver, Jan. 3-5. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Feb. 10. Chairman, Dr. Charles M. Bakewell, State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: *Examination.* Dover, July 9-11. *Reciprocity.* Dover, July 16. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, April 22-23. Sec., Dr. George C. Ruhland, 201 District Bldg., Washington.

GEORGIA: Atlanta, June. Joint-Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, April 2. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Jan. 23-25. Acting Superintendent of Registration and Education, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 18-20. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, Jan. 9. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, State Department of Health, Capitol Bldg., Des Moines.

KANSAS: Topeka, Dec. 12-13. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

MARYLAND: *Regular.* Baltimore, Dec. 12-15. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, Dec. 12-13. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: Ann Arbor and Detroit, June 12-14. Sec., Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 2-3. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Jan. 16-18. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: *Reciprocity.* Helena, April 1. *Examination.* Helena, April 2-3. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science.* Omaha, Jan. 9-10. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

NEVADA: *Reciprocity with oral examination.* Carson City, Feb. 5. Sec., Dr. Frederick M. Anderson, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: Concord, March 14-15. Sec., Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, June 18-19. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 8-9. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 29-Feb. 1. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: *Reciprocity and Endorsement.* Raleigh, Dec. 11. Sec., Dr. W. D. Jarvis, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 2-5. Sec., Dr. G. M. Williamson, 415 S. Third St., Grand Forks.

OKLAHOMA: Oklahoma City, Dec. 13. Sec., Dr. James D. Osborn, Jr., Frederick.

OREGON: *Basic Science.* Portland, Feb. 24. *Applications must be on file not later than Feb. 7.* Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, January. Dir., Bureau of Professional Licensing, Dr. James A. Newpher, Department of Public Instruction, 358 Education Bldg., Harrisburg.

PUERTO RICO: Santurce, March 5. Sec., Dr. O. Costa Mandry, Box 3854, Santurce.

RHODE ISLAND: Providence, Jan. 4-5. Sec., Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 16-17. Dir., Medical Licensure, Dr. G. J. Van Heuvelen, State Board of Health, Pierre.

TENNESSEE: Memphis, Dec. 20-21. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

VERMONT: Burlington, Feb. 13-15. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 13. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WISCONSIN: Madison, Jan. 9-11. Sec., Dr. E. C. Murphy, 314 E. Grand Ave., Eau Claire.

WYOMING: Cheyenne, Feb. 5. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

District of Columbia Reciprocity Report

Dr. George C. Ruhland, secretary, Commission on Licensure, reports nine physicians licensed by reciprocity on September 28 and October 18. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
George Washington University School of Medicine		(1935)	Georgia
Georgetown University School of Medicine		(1927)	Maryland
Howard University College of Medicine		(1929)	Ohio, (1935) North Carolina, (1936, 2) Virginia
Johns Hopkins University School of Medicine		(1937)	Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons		(1935), (1936)	Maryland

Indiana June Examination

Dr. J. W. Bowers, secretary, Indiana State Board of Medical Registration and Examination, reports the written examination held at Indianapolis, June 20-22, 1939. The examination covered fifteen subjects and included 100 questions. An average of 75 per cent was required to pass. One hundred and eight candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Loyola University School of Medicine		(1938), (1939)	2
Northwestern University Medical School		(1939)*	1
University of Illinois College of Medicine		(1939)	2
Indiana University School of Medicine		†, (1939, 98)	99
Harvard Medical School		(1939, 2)	2
Julius-Maximilians-Universität Medizinische Fakultät, Würzburg		(1922)	1
Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn		(1937)	1

* License has not been issued.

† This applicant has completed three years' work and will not receive his degree or license until 1940.

Rhode Island October Examination

Dr. Robert M. Lord, secretary, Rhode Island State Board of Examiners in Medicine, reports the oral, written and practical examination held at Providence, Oct. 5-6, 1939. The examination covered twelve subjects and included seventy-five questions. An average of 80 per cent was required to pass. Twelve candidates were examined, all of whom passed. Three physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Georgetown University School of Medicine		(1937)	1
Harvard Medical School		(1938)	1
Tufts College Medical School		(1937), (1938, 3)	4
New York Medical College and Flower Hospital		(1936)	1
Jefferson Medical College of Philadelphia		(1938)	1
Vanderbilt University School of Medicine		(1937)	1
University of Toronto Faculty of Medicine		(1937)	1
Université de Paris Faculté de Médecine		(1936)	1
Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia		(1935)	1

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Yale University School of Medicine		(1937)	N. B. M. Ex.
Tufts College Medical School		(1936), (1937)	N. B. M. Ex.

Vermont June Examination

Dr. W. Scott Nay, secretary, Vermont State Board of Medical Registration, reports the written examination held at Burlington, June 14-16, 1939. The examination covered twelve subjects and included ninety questions. Seventeen candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Johns Hopkins University School of Medicine		(1935)	86.8
University of Vermont College of Medicine		(1938) 86.1, 86.3, (1939)* 81, 85.1, 85.1, 85.7, 85.8, 87.7, 88.1, 88.2, 88.3, 89.1, 89.8, 90.8	
McGill University Faculty of Medicine		(1936)	86.1
University of Edinburgh Faculty of Medicine		(1935)	86.5

Six physicians were licensed by endorsement from February 8 through July 14. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard Medical School		(1932), (1935)	N. B. M. Ex.
Tufts College Medical School		(1936)	N. B. M. Ex.
University of Nebraska College of Medicine		(1937)	Nebraska
University of Vermont College of Medicine		(1933)	N. B. M. Ex.
University of Edinburgh Faculty of Medicine		(1937)	N. B. M. Ex.

* Licenses have not been issued.

Book Notices

Pneumonia with Special Reference to Pneumococcus Lobar Pneumonia. By Roderick Heffron, M.D., Medical Associate, the Commonwealth Fund. Cloth. Price, $4.50. Pp. 1,086, with 18 illustrations. New York: Commonwealth Fund; London: Oxford University Press, 1939.

The medical profession is indebted to Dr. Heffron for this scholarly volume on pneumonia, published by the Commonwealth Fund at a price permitting wide distribution. It is a well conceived and splendidly executed monograph of permanent value. Our current knowledge of pneumonia in the clinic, in the laboratory and in the community is presented with evident diligence, careful documentation and balanced judgment in twenty chapters dealing with causative organisms in pneumonia and pneumonia not due to pneumococci, the pneumococcus and type incidence in pneumonia, pathology of lobar pneumonia, aspects of immunity, experimental pneumococcic infections and pathogenesis of lobar pneumonia, epidemiology, measures for the prevention of pneumonia, symptoms of lobar pneumonia, physical signs in lobar pneumonia, clinical varieties of pneumonia and association with other conditions, special features in the course of the disease, complications, incidence and treatment, diagnosis, differential diagnosis, prognosis, recovery factors and duration of immunity, general therapeutic measures, serum treatment, results of serum treatment and continuing problems. In spite of the wealth of information presenting our current knowledge of the pneumonias, advances in this field appear so frequently that new editions or supplements may be expected. Sulfapyridine has greatly augmented our capacity to treat the pneumonias and their complications. The whole problem of sulfapyridine fastness has developed since the book went to press. The relative places of sulfapyridine and of serum in therapy are still *sub judice* and the appropriate use for each must be determined. In a comprehensive presentation, the choice of data for inclusion is at times a matter of fine discrimination, which has been well exercised by Dr. Heffron. Nevertheless greater elaboration of the subject of radiographic diagnosis and mention of the significance of lobar segments (described by Kramer and Glass) would have been advantageous. The work of Jacob Fine and others in connection with the treatment of abdominal distention with oxygen is not mentioned nor that of Lamar in connection with the influence of antibody on the lysis of pneumococci. Certain clinical anatomic terms have been saved from oblivion, such as "apical pneumonia," "abortive," "central" and "terminal"; these might well have been "liquidated" in the interest of the etiologic classification, which dominates the volume. The statement that "clinical differentiation of bronchopneumonia from lobar pneumonia is usually not difficult" is not in accord with the experience of many clinicians. The criteria offered for differentiation are not adequate, especially for the infections of children. Of great value is the well selected and inclusive bibliography. The convenience of the excellent index would be enhanced if more synonyms were listed and if there were more cross references. Because it is a thoroughly reliable source book on an important and developing topic of general medical interest and a model of logical presentation, this volume should be on the "must" list of all who provide books for students and practitioners of medicine.

A Descriptive Atlas of Radiographs: An Aid to Modern Clinical Methods. By A. P. Bertwistle, M.B., Ch.B., F.R.C.S. Fourth edition. Cloth. Price, $15. Pp. 576, with 852 illustrations. St. Louis: C. V. Mosby Company, 1939.

The author seeks to furnish a pictorial reference book of those normal and abnormal conditions which are met more commonly in practice; rare lesions are omitted, except when of special interest. The volume is primarily intended for the use of the clinician, whose chief concern is diagnosis. No special technical knowledge is required in using this atlas. The illustrations, on the whole, are excellent. Some, however, are too small or have lost detail in reproduction and fail to demonstrate the lesion. Most of the roentgenograms are accompanied by diagrammatic sketches, which depict the lesion under consideration. The small size of these outline drawings, the rather crude sketching and the almost illegible microscopic lettering detract greatly from the effectiveness and value of the diagrams. Standardization of presentation would facilitate the reader's orientation in examining films. For example, the chest films show the heart either on the left or on the right; the stomach and gallbladder pictures are likewise either in the accepted anteroposterior view or in reverse position. Figure 21 and its accompanying diagram are in mirror-image relationship. Fractures are overemphasized in a series of 112 roentgenograms, whereas the vascular system commands only thirteen illustrations; there is no cardiac section. A number of diagnoses are questionable (for example, chronic appendicitis; congenital coxa vara is called Legg-Perthe-Calvé's disease in figure 66; the history and roentgenograms accompanying figures 75 and 76 suggest recovery from paraplegia resulting from cord compression in tuberculous spondylitis rather than spina bifida; the examples of acute osteomyelitis show enough late changes to be considered subacute or chronic. Only a few errors of composition were found. Figure 611 is upside down. Figures 830-834 are grouped without individual identification. The name of Dr. Legg is misspelled "Legge." Despite the foregoing criticisms, the atlas fulfils its purpose to a large degree in providing the general practitioner with a handy reference volume of radiographic interpretation of common lesions.

Sclerosing Therapy: The Injection Treatment of Hernia, Hydrocele, Varicose Veins and Hemorrhoids. Edited by Frank C. Yeomans, M.D., F.A.C.S., M.R.S.M., Professor of Proctology and Attending Surgeon, New York Polyclinic Medical School and Hospital, New York. Cloth. Price, $6. Pp. 337, with 185 illustrations. Baltimore: William Wood & Company, 1939.

Sclerosing therapy has emerged from the stage of experiment and empiricism. For a long time the domain of itinerant quacks and misunderstood pioneers, it is now taking a definite place in the hands of well trained physicians whose experience is not limited to this form of treatment. It is not the possession of a syringe and needle that qualifies the general practitioner to use such methods but a thorough understanding of the nature of the disease whose treatment by injection has been assembled in this group of four monographs.

The first of these, on the injection treatment of hernia by Bratrud, is perhaps the least convincing and encouraging. In spite of his careful selection of cases and surely an excellent technic, he reports recurrences in bilateral, indirect inguinal hernias in 31 per cent, the direct inguinal hernias giving a recurrence rate of 40 per cent. This, in the light of our present surgical methods, using silk and local anesthesia, is far too high. The microscopic sections showing proliferation of fibroblasts and extensive fibrosis occluding the hernial openings reveal nothing of the tensile strength of such tissue. Unless such studies become known, one will have to suspect that this fibrous tissue gives way and splits up easily, especially when more five year cures are known. The chapter on trusses is valuable and instructive. That old, handicapped patients who have trouble retaining their hernias with a well fitting truss may do so after a series of injections is a point well taken. While the author has taken a conservative attitude in his indications, further restrictions are bound to come when the limitations of this method are more clearly recognized. Obviously, the general practitioner will be tempted to try such a method instead of a surgical dissection, but this is justified only if his results are not inferior. This has not been shown by the data presented.

The discussion of the injection treatment of hydrocele by Dr. George J. Hoch is short, concise and entirely adequate. He advocates the use of quinine and urea hydrochloride and carefully lists the contraindications to its use.

The monograph on the injection treatment of varicose veins has been written by Harold J. Shelley and is undoubtedly the best monograph on this subject. He has not only completely covered the important literature but shows a complete familiarity with all the aspects of treatment, which permits him to choose or combine surgical methods with treatments by injection.

The fourth treatise on the injection treatment of hemorrhoids is written by Dr. Frank C. Yeomans, one of the most experienced proctologists of the country. He makes it clear that only uncomplicated, internal hemorrhoids should be injected, which comprise about 50 per cent of all cases. The solution preferred is phenol. He stresses the fact that the injections are made in the submucous or interstitial tissues and not into

blood vessels and thus the requirements for a successful solution differ from those used in the treatment of varicose veins.

The printing and illustrations are excellent; the language of the monograph on hernia is careless and contains a few errors in printing. The book is strongly recommended for the general practitioner as a preliminary study followed by guided clinical experience.

Les embolies cérébrales: Études de pathologie expérimentale sur les embolies solide et gazeuse du cerveau. Par Maurice Villaret, professeur à la Faculté de médecine de Paris, et René Cachera, médecin des hôpitaux de Paris. Paper. Price, 32 francs. Pp. 134, with 89 illustrations. Paris: Masson & Cie, 1939.

With the help of a window in the skull of dogs, the authors observed and photographed the pial vessels with a magnification which enabled them to study the arteriolar system and its reaction to cerebral emboli. Solid emboli were produced by the introduction of finely pulverized marble or glass with particles from 80 to 150 microns in diameter into the carotid artery. The immediate reaction to such emboli was a widespread arteriolar spasm, which was present even at a distance from the plugs. These observations were made from the time of embolization up to three hours. In another group of experiments the late vasomotor disturbances from one to 123 days after the embolism were studied. Again there were marked vasospastic phenomena alternating with areas of vasodilatation; the current in the veins was retarded and sometimes reversed. The authors also studied the development of collateral circulation and the "in vivo" appearance of cerebral infarcts. In the second series air was introduced either in the pulmonary vein or in a systemic vein; the vascular system of the pia mater, however, did not react with any vasomotor disturbances to the plugs of air; it simply caused a mechanical obstruction with its natural consequences. In one instance a simple puncture of a pulmonary vein resulted in a demonstrable air-bubble in one of the pial vessels. The authors also presented evidence that air introduced through the saphenous vein may pass through the pulmonary bed and produce cerebral air embolism. Eighty photomicrographs of the pial vessels illustrate the monograph. They convincingly demonstrate the disturbed vasomotricity of the cerebral vessels. The original method of Forbes has been employed here to add to the understanding of cerebral vascular accidents. While the authors do not attempt any clinical deductions, the application of this knowledge to clinical cases of cerebral embolism and possibly other vascular accidents is stimulated. For the physiologist, neurologist and men engaged in research on the vascular system the book is strongly recommended.

John Howard (1726-1790) Hospital and Prison Reformer: A Bibliography. By Leona Baumgartner, M.D., Ph.D. With introduction by Arnold M. Muirhead, M.A. Reprinted from Bulletin of the History of Medicine, Vol. VII, No. 5 and No. 6, 1939. Boards, Price, $1. Pp. 79, with 9 illustrations. Baltimore: Johns Hopkins Press, 1939.

John Howard became interested in conditions in prisons when, shortly before the age of 50, he was appointed high sheriff of Bedfordshire. On attempting to correct prison abuses, he was told that there was no precedent for the expense to be incurred. "I therefore rode into several neighboring counties in search of one; but I soon learnt that the same injustice was practiced in them; and, looking into the prisons I beheld scenes of calamity which I grew daily more and more anxious to alleviate. In order therefore to gain a more perfect knowledge of the particulars and extent of it by various and accurate observations I visited most of the county gaols in England." Howard extended his observations to the prisons and hospitals on the continent and published his reports under the general title of "The State of Prisons in England and Wales . . . and an account of some Foreign Prisons," which passed through a number of editions. The present volume is the bibliographic record of these editions and appended reports, reprinted from the Bulletin of the History of Medicine VII, Nos. 5 and 6, 1939, together with a biographic note on Howard by Arnold M. Muirhead, whose collection of Howardiana contributed to the completeness of the bibliographic material. There are added sections on biography and criticism, and on contemporary biographic notes and reviews. Howard's method of bringing about reform was to ascertain and publish the facts. The justice of his cause and the value of his efforts were recognized by his contemporaries, but little headway toward improvement was made against precedent and custom during his lifetime. A contemporary reviewer (1789), commenting on Howard's lazarettos, reflects the current opinion of his time, somewhat pessimistic but perhaps more prophetic than he knew. "His idea of a perfect hospital contains much (we suspect, very useless) refinement but as it is the refinement of Mr. Howard we shall subscribe to it. . . . On the whole the volume contains many facts of importance and many observations of real utility . . . and we leave it with the best founded expectations that our author's past and future labors will not be wholly in vain." This book is an excellent piece of bibliography.

Étude toxicologique, physiologique et histophysiologique de l'hémoglobine en solution administrée à dose thérapeutique par voie veineuse à des chiens en état d'anémie aiguë par saignée. Par le Docteur Raymond Castagnou, docteur en pharmacie. Paper. Pp. 405, with 58 illustrations. Bordeaux: Imprimerie E. Drouillard, 1939.

This book, in organization and content, resembles a doctor's thesis as the term is understood in the United States. It consists almost entirely of experimental data obtained from a series of fifty-three dogs which were first exsanguinated and then given transfusions with solutions of canine or equine hemoglobin. The object of the study was to ascertain whether solutions of either homologous or heterologous hemoglobin could be used in the treatment of anemia from acute hemorrhage. Extensive data on the freezing-point depression, surface tension, specific gravity, viscosity, osmotic pressure, hydrogen ion concentration and electrolyte content of hemoglobin solutions are given. It was found that such solutions were toxic to many animals, producing mild azotemia with recovery or oliguria and uremia with fatal outcome. An acute syndrome sometimes occurred characterized by collapse, vomiting, diarrhea, hemorrhages from the entire gastrointestinal tract, and death within a few hours. In his toxicologic studies the author, curiously enough, ignored the experimental work of Yorke and Nauss, Baker and Dodds, and DeGowin, Osterhagen and Andersch, which demonstrated a relationship between the reaction of the urine and the occurrence of renal insufficiency from hemoglobinuria. He studied the disappearance of hemoglobin from the blood stream by quantitative estimations of the hemoglobin in the urine and analysis of iron in the various organs. From 2 to 54 per cent of the pigment was excreted in the urine, while the organs most concerned in retaining the iron were the spleen, lungs, liver and kidneys in order of activity. By means of blood gas analysis the author demonstrated that the transfusion of hemoglobin solutions could replace blood as a vehicle for gaseous exchange for from eight to twenty-four hours but that the time was limited by the excretion or immobilization of the hemoglobin. It is also admitted that the toxicity of the hemoglobin solutions is a further disadvantage in applying such a procedure clinically. The illustrations are all photomicrographs of kidneys, lungs and livers showing reactions from hemoglobin. The extreme length of the publication is partly due to the fact that the detailed protocols of individual animals sometimes occupy three or four pages. The book should be of interest to workers in the field but contains little that can be applied clinically.

Elements of Statistical Reasoning. By Alan E. Treloar, Ph.D., Associate Professor of Biostatistics, University of Minnesota, Minneapolis. Cloth. Price, $3.25. Pp. 261, with illustrations. New York: John Wiley & Sons, Inc.; London: Chapman & Hall, Limited, 1939.

"Every set of factual data in science that may be assembled for statistical analysis presents questions which are intimately concerned with the validity of the data themselves. Misinterpretation all too readily flows from routine application of statistical procedures. . . . That which comprises good health at one age may quite properly be regarded as poor health at another age. It is virtually impossible to reach general concordance of judgment in subdividing variation in the state of health into even very few subgroups. . . . The accuracy of mathematical deductions from data must inevitably be limited in some way by the precision and adequacy of the observations themselves. Emphasis must always be laid, therefore, on the necessity for the exercise of critical judgment in the collection

and recording of data. Precision in measurement and care in classification materially enhance the value of observations."

In statements such as these does the author of this addition to discussions of the statistical method in science emphasize the importance of the fundamental data on which the statistical reasoning is based. The present frequency of biologic and medical papers with a statistical bias indicates the need for constant review of the fundamental facts which serve as their basis. In other respects also the author has satisfactorily considered the methodology of statistics as applied to most of the problems faced by the biologist. The mere publication of books on this subject is in itself evidence of at least potential demand; indeed, courses in this field might well be required in the preclinical years, supplemented by practical application during later phases of the medical curriculum.

Varicose Veins. By Alton Ochsner, B.A., M.D., D.Sc., William Henderson Professor of Surgery and Director of the Department of Surgery, School of Medicine, Tulane University of Louisiana, New Orleans, La., and Howard Mahorner, B.A., M.D., M.S., Assistant Professor of Surgery, School of Medicine, Tulane University of Louisiana. Cloth. Price, $3. Pp. 147, with 52 illustrations. St. Louis: C. V. Mosby Company, 1939.

The subject of varicose veins is admirably covered in this authoritative, concise monograph. With the help of excellent diagrams and photographs, the authors have not only given a complete history of the treatment of varicose veins but have reviewed the anatomy, pathology, physiology, etiology, clinical aspects, examination and treatment of the patient suffering from varicose veins and ulcers. The book is dedicated to Rudolph Matas, "universally acclaimed father of vascular surgery," who wrote an interesting foreword. It is gratifying to see that from the hands of itinerant quacks and a few zealous pioneers this subject is now taken over by surgical teachers of international reputation, whose didactic skill and original research have been so well incorporated to produce the first real textbook in this field. One point should be emphasized in recommending this book to the general practitioner: The injection treatment of varicosities is technically so easy that it has become widely popular with the medical profession. This monograph dwells at length on appropriate diagnostic tests which permit the formulation of a rational therapy. This almost invariably includes a combination of ambulatory ligations at the proper levels with the injections. The wholesale and uncritical injections into dilated veins have often discredited the treatment and incurred unnecessary loss of time and expense for the patient.

The Anatomy of the Nervous System from the Standpoint of Development and Function. By Stephen Walter Ranson, M.D., Ph.D., Professor of Neurology and Director of Neurological Institute, Northwestern University Medical School, Chicago. Sixth edition. Cloth. Price, $6.50. Pp. 507, with 382 illustrations. Philadelphia & London: W. B. Saunders Company, 1939.

In this edition of Ranson's well known and excellent textbook on neuro-anatomy there has been extensive revision in various chapters without material enlargement. The connections of the thalamus with the cortex, brachium conjunctivum, medial lemniscus, spinothalamic tract and secondary trigeminal tracts are discussed in detail. As in the past, emphasis has been on the developmental and functional significance of structure. There are twenty-one chapters. There is a laboratory outline of neuro-anatomy with clinical illustrations. There is an excellent bibliography. The illustrations are beautiful and excellently labeled. Every student as well as every neuropsychiatrist, neurophysiologist and neuro-anatomist should have this book.

Rural Medicine. Proceedings of the Conference Held at Cooperstown, New York, October 7 and 8, 1938. Cloth. Price, $3.50. Pp. 268. Springfield, Illinois & Baltimore: Charles C. Thomas, 1939.

Although this was primarily a local conference centering about the activities of the Mary Imogene Bassett Hospital at Cooperstown, N. Y., the speakers were drawn from a wide circle. There were four subjects under discussion: rural morbidity, health department programs and school health programs in rural areas, postgraduate medical education in rural areas, and economics of rural medicine. In spite of a well organized program with a wide variety of speakers, the proceedings of the conference are not simply a presentation of divergent views, lacking in continuity and comprehensiveness. The material assembled under these various heads constitutes valuable material for the study of the problems of rural medicine. It may be significant of an advance in the discussion of medical problems that no speaker attempted to present a panacea. The rather extensive bibliography on rural medicine that is included can hardly be considered either adequate or impartial, but it is at least a beginning which should form a basis for a more complete bibliography.

Die Diät- und Insulinbehandlung der Zuckerkrankheit für Studierende und Ärzte. Von Dr. Franz Depisch. Mit einem Vorwort von Prof. Dr. N. v. Jagić. Second edition. Paper. Price, 4.80 marks. Pp. 155, with 10 illustrations. Vienna: Julius Springer, 1939.

The author stresses the importance of proper diet in treatment of diabetes, emphasizing the fact that the use of insulin without regard to diet is sometimes harmful. That the cost of insulin to the individual and to institutions is often prohibitive is alone a reason for greater importance being attached to diet, plus the fact that diet is at times even more vital than insulin, are everywhere stressed by the author. It is felt, of course, that the economic side must be considered, but one cannot go as far as the author when he insists that doctors should use insulin sparingly. Certainly the good of the patient and not the cost of the treatment is the first consideration. The author stresses the importance of insulin and protamine zinc insulin being used only by doctors with a thorough knowledge of their therapy. He makes special mention of surfen, a new slow-acting insulin of which we know little in this country because of its failure yet to be introduced into our clinics. Dr. Depisch discusses thoroughly what most of us already know—the preventive side of diabetes by treatment for obesity. At the end of each chapter is a summary pointing out the high lights and making the book simpler to read and to understand. At the end of the book is an excellent summary. A careful reading of this book is a requisite to doctors and medical students.

Gregg Medical Dictation Series: A Course for the Student Who Desires to Become Proficient in Taking Medical Dictation. Volume I: General Medicine. Volume II: Surgery. Volume III: Pediatrics. By Marie Zweegman Yates, Director, Zweegman School for Medical Secretaries, San Francisco, California. Experimental edition. Paper. Price, $1 per volume. Pp. 90; 88; 89. New York: Gregg Publishing Company, 1939.

When completed, this series will comprise sixteen volumes. Three volumes have now been issued, each a complete unit devoted to a single phase of the subject, such as general medicine, surgery and pediatrics. The object is to acquaint the student with the vocabulary of the subject treated and to present the easiest means of transposition into shorthand symbols. For this purpose, case histories are given in each volume, as well as a glossary containing pronunciations and definitions of words appearing in the Eighteenth Edition of the American Illustrated Dictionary by Dorland, and the Gregg shorthand outlines for them. The series should be most helpful to those for whom it is being prepared.

Elementary Anatomy and Physiology. By James Whillis, M.D., M.R., F.R.C.S., University Reader in Anatomy, Guy's Hospital Medical School, London. Foreword by T. B. Johnston, M.D., Ch.B., Professor of Anatomy, University of London. Cloth. Price, $3.50. Pp. 342, with 87 illustrations. Philadelphia: Lea & Febiger, 1939.

This is a well balanced elementary treatment of the anatomy and physiology of the body. The text is clearly written and the diagrams and drawings are well designed to make clear to the beginner the main facts of structure of the human body. The physiologic facts presented should enable the student to begin to think of organs to some extent in terms of their functions. Both anatomy and physiology are presented in too elementary a fashion to make the book of much value to American medical students, in view of the organization of courses in these subjects in the United States. It should, however, meet a real need in premedical courses and especially in courses in nursing education. If medical students could enter the first year of the medical course with the knowledge of anatomy and physiology which this book would give them, they could go on to gain a detailed knowledge of the body much more easily than is now true for the majority. Numerous books have appeared in recent years with the avowed purpose of simplifying or abbreviating anatomy. The present volume seems to have accomplished these purposes well for the beginner, while making it obviously necessary for the more advanced student to seek more complete textbooks.

Die Behandlung von Hauttuberkulosen an der Giessener Lupusheilstätte 1937/38. Von Dr. Adolf Kreiner. Mit einem Geleitwort von Prof. Dr. W. Schultze, Leiter der Lupusheilstätte Giessen. Nr. 73, Tuberkulose-Bibliothek, Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- u. Obermedizinalrat, Berlin, und Dr. Karl Diehl, dirigierender Arzt, Sommerfeld. Paper. Price, 6 marks. Pp. 61. Leipzig: Johann Ambrosius Barth, 1939.

In this monograph the author reports his experiences in the treatment of 536 cases of cutaneous tuberculosis, chiefly lupus. The advantages of grenz ray therapy over x-rays are stressed even though the cosmetic results were not always satisfactory. From three to five doses of 4,000 roentgens per field with 9 kilovolts, 20 milliamperes, were found to give the best results. In most cases this treatment was preceded by operative removal of the lupus foci with the electric cutting current, a wire loop being used to remove the entire area with a margin of healthy skin. The treatment is painful and requires local anesthesia and careful after-treatment. Contact therapy with ultraviolet radiation from a water-cooled quartz mercury vapor arc lamp either alone or preceded by electrical ablation is used in lupus in children and in cases that had been previously treated with roentgen rays or radium. Old tuberculin (Koch) is used as an adjunct beginning with minute doses (0.1 cc. of 1:1,000,000 dilution) and is especially effective in papulonecrotic tuberculids. Dietetic treatment with a salt poor, high vitamin diet is not recommended on account of the long duration of the treatment and the expense. Photographs of patients have unfortunately been omitted so that it is difficult for the reviewer to appraise the cosmetic results.

Studies From the Center for Research in Child Health and Development, School of Public Health, Harvard University. I: The Center, the Group under Observation, Sources of Information, and Studies in Progress. By Harold C. Stuart, M.D., and Staff. Monographs of the Society for Research in Child Development, Volume IV: No. 1 (Serial No. 20). Paper. Price, $1.75. Pp. 261, with illustrations. Washington, D. C.: Society for Research in Child Development, National Research Council, 1939.

This small monograph contains a description of the research and progress at the Center for Research in Child Health and Development at the Harvard School of Public Health. The organization of the center is given in detail, both the physical facilities and the composition of the staff being enumerated. Types and methods of examination are fully outlined and charts are included to indicate the types of dietary information obtained as well as physical data derived from the subjects under study. This monograph is well illustrated, showing the various instruments used for taking the physical measurements. Several family studies are given in detail and are illustrated with photographs and charts. This monograph should be of great interest to those engaged in similar studies.

Histopathology of the Tooth and Their Surrounding Structures. By Rudolf Kronfeld, B.S., M.D., D.D.S., Professor of Dental Histology and Pathology in the Chicago College of Dental Surgery, School of Dentistry, Loyola University, Chicago, Illinois. Second edition. Cloth. Price, $7. Pp. 504, with 438 illustrations. Philadelphia: Lea & Febiger, 1939.

This is a thorough revision of the first edition, which has been completely rewritten with the inclusion of much new material. Many of the changes in arrangement and content are such as to conform with the recommendations of the Report of the Curriculum Survey Committee of the American Association of Dental Schools. Some of the material included is not strictly histologic in character, as, for example, the first two chapters, on anomalies in the shape and size of the teeth and the physiology and pathology of tooth calcification. This departure is highly commended; indeed, the second chapter should be read carefully by all scientists and practitioners of both medicine and dentistry interested in tooth calcification. The content is liberally inclusive and is a thoroughly adequate presentation of the subject as indicated by the title. The descriptive material is liberally supplemented by well chosen illustrations which are also almost technically perfect. At the close of each chapter is a carefully selected bibliography of the more pertinent articles bearing on that part of the subject. The nomenclature and classification of gingivitis and pyorrhea used by the author are those of Gottlieb; from the point of view of the clinician this is both confusing and unsatisfactory, in spite of the table on pages 316 and 317 differentiating the various forms. However, simplification and clarification of this situation continues to be a problem awaiting solution. The influence of the enamel cuticle in protecting the tooth from the onset of dental caries (page 106) would seem to be overemphasized. The implied acceptance of Bunting's opinion that the only significant difference thus far known between caries-free and caries-susceptible persons is in the number of Bacillus acidophilus organisms in the mouth is hardly justified in the light of current chemical research. In spite of these and possibly other minor criticisms, this is without doubt the leading textbook in this field in the English language.

German-English Science Dictionary for Students in the Agricultural, Biological and Physical Sciences. By Louis De Vries, Professor of Modern Languages, Iowa State College, Ames. With the collaboration of Members of the Graduate Faculty. Fabrikoid. Price, $3. Pp. 473. New York & London: McGraw-Hill Book Company, Inc., 1939.

The author of this German-English science dictionary received the cooperation of many of his colleagues in its compilation. The number of sciences that had to be studied necessitated a rigid selection of words. Not all the names of animals, plants, insects or chemical compounds have been included. These omissions will of necessity impair somewhat its usefulness but no doubt some of them will be corrected in future editions.

An Introduction to Modern Genetics. By C. H. Waddington, Sc.D., Fellow of Christ's College, Cambridge. Cloth. Price, $4. Pp. 441, with 160 illustrations. New York: Macmillan Company, 1939.

The aim of this book is to give an account of the more important recent developments in the field of genetics. Although the literature on the subject is most extensive, the author has succeeded in presenting a relatively brief account. On the whole, however, the book seems more suitable for collateral reading in connection with a college or university course in genetics than for the general perusal of the casual reader even when possessed of considerable biologic background. To the physician the brief chapter on human genetics is naturally the most interesting.

Peripheral Vascular Diseases: Diagnosis and Treatment. By William S. Collens, B.S., M.D., Chief of the Clinic for Peripheral Vascular Disease, Israel Zion Hospital, Brooklyn, and Nathan D. Wilensky, M.D., Assistant in Clinic for Peripheral Vascular Disease, Israel Zion Hospital. Cloth. Price, $4.50. Pp. 243, with 77 illustrations. Springfield, Illinois, & Baltimore: Charles C. Thomas, 1939.

This monograph has been written to offer the physician a reference work which may aid him in the management of peripheral vascular disease. For the most part this task has been accomplished. Some of the chapters, such as the one on peripheral vascular sclerosis, follow closely the teachings of Winternitz, are beautifully presented and are profusely illustrated. Other subjects, such as congenital vascular anomalies, aneurysms and varicose veins, are hardly mentioned. The surgical treatment of acute arterial embolism is not encouraged. The classification of peripheral vascular disorders is somewhat cumbersome and overlapping. While certain tests and apparatus which the authors have devised are treated in great detail, others are less favorably treated, which gives the unbiased reader a feeling of false proportions. The design and printing of the book and the colored plates satisfy the highest standards of medical publications.

Dentistry for Children. By John Charles Brauer, D.D.S., A.B., M.Sc., Head of Department of Preventive Dentistry, University of Iowa School of Dentistry, Iowa City. With Special Chapters by L. B. Higley, B.A., D.D.S., M.S., Professor, and Head of Department of Orthodontics, School of Dentistry, University of Iowa, and Julian D. Boyd, M.S., M.D., Associate Professor of Pediatrics, College of Medicine, University of Iowa. Cloth. Price, $6.50. Pp. 373, with 335 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1939.

This book considers the many problems found in the modern dental office. The subjects are presented in a concise manner, and special mention is due the illustrations, which are so carefully presented as to make many pages of interesting study. There is sufficient review of the basic anatomy and structural parts to be interesting, but the author does not "fill in" with lengthy reviews. Instead, the newer more vital subjects in connection with preventive dentistry together with chapters devoted to instructive suggestions in managing the child patient are thoroughly treated. Also the correlation of the author's writings with those of the orthodontist and the pedia-

trician insures thorough coverage of the subject from every available angle. Chapter 9, devoted to preventive orthodontics, is actually saturated with helpful suggestions for the solution of the problems of the general practitioner. The illustrations and explanations offered in this chapter would be exceedingly fine for the practicing dentist to have available in his office for more fully explaining to the public their various problems. The book is highly recommended to the student as a textbook, to the practicing dentist as a reference book, and to both as an indispensable guide for better understanding the unique field of children's dentistry.

Die Zuckerkrankheit. Von Prof. Dr. Wilhelm Falta. Second edition. Paper. Price, 7 marks. Pp. 154. Berlin & Vienna: Urban & Schwarzenberg, 1939.

This little manual on diabetes includes discussions of diagnosis, differential diagnosis, pathogenesis, dietetic management, complications and the use of the old and newer insulins. It reflects largely the views of its author. For American readers the excellent books available in English will probably prove more useful.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Alleged Negligence in Treatment of Chest Wound by "Visiting Surgeon" of Hospital.—The plaintiff, by his next friend, sued the defendant physician to recover damages for alleged malpractice. The trial court directed a verdict for the defendant and thereafter reported the case to the Supreme Judicial Court of Massachusetts on a stipulation of the parties.

When about 11 years old the plaintiff, in the early part of January 1935, was injured while coasting. A runner of the sled of another boy struck him, went through his clothing and made a wound in his chest. He was brought to a hospital, where he was examined by the defendant, who was "visiting surgeon," and another physician who was "house officer." The defendant directed the taking of roentgenograms, the results of which were negative. Under his direction, the wound was washed with "green soap" and closed by sutures, and antitoxin was injected in the patient's arm. The patient remained in bed at the hospital for nine days, during which period he was treated daily by the "house officer" and seen by the defendant on his daily rounds of the hospital. After an eleven-day stay he went home on January 14 and thereafter for a period of about two months visited the outpatient department of the hospital weekly and was treated by the "house officer." During this period, pus appeared in the wound and on two occasions the "house officer" picked from it some threads. At the end of three months the wound was only partially healed and the patient was taken to another hospital where an examination disclosed a chronic sinus of the chest wall from which was removed a small piece of wool fabric. Two weeks thereafter the wound had healed.

The defendant's evidence tended to show that on examining the patient at the time he entered the hospital the defendant found a lacerated wound over the left breast. The chest wall was exposed and there was some bleeding. The defendant directed the "house officer" to give the treatment earlier described, admonishing him to be careful in any scraping of the wound because the chest wall was so thin. The purpose of the treatment directed and given was to get out all the foreign material possible, to give anything left in the wound room to get out, and to drain and help evacuate the wound of pus or foreign material. The defendant never saw the patient after he left the hospital. The defendant testified that when the patient left the hospital the wound was discharging serum, not pus, and that such a wound would take three or four months to heal; that the treatment given was good surgical treatment and that no more could have been done at the hospital than was in fact done.

Viewing all the evidence in the case in the light most favorable to the patient, the court said, a basis was not afforded for finding the defendant negligent. The precise relationship between the defendant and the "house officer" was not disclosed by the record but an inference was warranted, in the opinion of the court, that it was the latter's duty to administer to patients such treatment as the defendant directed. There was nothing in the record to indicate that the defendant had anything to do with the outpatient department or had any supervision over treatment there given to patients. The patient contended that the defendant was negligent in not discovering and removing from the wound, at the time of the examination, the bit of wool fabric which was removed several months later. If the testimony of the defendant were accepted, the court said, there was adequate reason for not ascertaining at that time whether any foreign matter was in the wound, and the course followed by the defendant of awaiting the partial healing of the wound and the formation of a sinus was prudent and proper. If his testimony were rejected, there was no expert testimony on which to base a finding that the conduct of the defendant was improper.

The fact that pus appears in a wound which is being treated by a physician does not warrant the finding that he was negligent; infection may arise regardless of the care used by the attending physician. There was here no evidence that the pus was seen before the patient left the hospital on January 14. There was no evidence of any specific act of the defendant or of the "house officer" that introduced any septic matter into the wound. The inference was warranted, the court continued, that foreign matter caused the appearance of pus but not at a time when the defendant was treating the patient or was supervising his treatment. Pus appeared while the patient was being treated in the outpatient department. The defendant had nothing to do with that department.

Since the evidence in the case did not warrant the submission of the case to the jury, judgment was entered for the defendant.—*Tallon v. Spellman (Mass.), 19 N. E. (2d) 33.*

Accident Insurance: Death from Chloral and Bromide Poisoning as Accidental.—The insurance company promised to pay to the beneficiary certain benefits if the insured died from bodily injuries effected directly and independently of all other causes through external, violent and accidental means which produced a visible contusion or wound on the exterior of the body. The insured died as a result of taking a medicinal compound containing cannabis, chloral hydrate, potassium bromide and extract of hyoscyamus. The company refused to pay the benefits and the beneficiary sued and obtained judgment in the trial court. The company then appealed to the court of appeals of Tennessee, western section.

The insured was so constituted physically that a comparatively small quantity of intoxicating liquor, while not making him drunk, would result in his being rendered highly nervous after the effect had worn off. To relieve this condition, which occurred at irregular periods only, he was accustomed to taking the medicine described, which he procured at a drug store without a physician's prescription. On the evening of Nov. 27, 1936, the insured had several drinks of gin and beer. He was not rendered noticeably intoxicated but nevertheless was so nervous the following day that he remained in bed. That night his wife telephoned to a neighborhood drug store and ordered some of the medicine. A 2 ounce (60 cc.) bottle of it was sent, with directions written on it to take "two teaspoonsful as needed." The insured was given a dose at 7:30 p. m. and another dose of 2 teaspoonfuls about midnight. He apparently took some more of the medicine about 12 noon of the following day and another dose of 2 teaspoonfuls about 3 o'clock. About 6:30 p. m. his wife noticed that he had a peculiar look about his eyes—that his eyes "looked kind of glassy"—and called in a friend of the family. Shortly after the arrival of this friend, the insured took another dose of the medicine (just how much does not appear in the record), staggered back to his bed, lay down on it and went into a deep sleep. A physician was immediately summoned and found the insured in a serious condition. "He had a pallor and his pulse was thready and weak, respiration shallow." The insured was immediately taken in an ambulance to a hospital where his

stomach was washed out and he was given cathartics and epinephrine. He died while on the emergency table, death being attributed to chloral and bromide poisoning resulting from the cumulative effect of the medicine.

The insurance company, in refusing to pay the benefits, insisted that the death was the natural result of an act in which the insured intentionally engaged and that therefore it was not accidental. The appellate court, however, was unable to agree to the contention that the insured actually took what he intended to take. True, the court said, he intended to take the identical liquid which he took, and it may be in precisely the quantity intended. It was clear to the court, however, that in so doing he meant to take a harmless "nerve remedy" and, based on his previous experience, thought that was what he was doing, whereas what he in fact took, instead of being harmless, was poisonous in the quantities taken. His ignorance of this fact introduced an entirely unforeseen and unexpected element into an act which was in other respects intentional, and hence rendered it "accidental."

The insurance company further contended that there was no proof of a visible contusion or wound on the exterior of the insured's body evidencing the injury that caused his death and hence recovery was not warranted even though the injury was effected by accidental means. The beneficiary insisted that the evidence was sufficient to meet the requirements of the policy, stressing the facts that when the insured staggered to the bed after taking the last dose of the medicine he lay down "and went into a deep sleep and his mouth flew open and he snored," that his features were "very white" and that "his head was drawn back." The words "contusion" and "wound," said the court, are of well known, commonly understood import which must be given effect. To the court there was no reasonable basis for the view that a pallid face and drawn head are within that meaning.

The judgment of the trial court for the plaintiff was therefore reversed and the case remanded for a new trial.—*Travelers Ins. Co. v. Ansley (Tenn.), 124 S. W. (2d) 37.*

Optometry: Duty of Optometrist to Detect Disease of Eye; Liability of Corporate Employer of Optometrist.—The defendant jewelry and optical corporation operated a department, in charge of a licensed optometrist, wherein the eyes of customers could be examined and glasses prescribed. The plaintiff's eyes had been hurting her for some time and on seeing the defendant's advertisement in a newspaper, she visited the optometrist in charge of the department, May 17, 1935. The optometrist examined her eyes and prescribed lenses which, however, failed to relieve the condition. On several occasions, according to the testimony introduced on her behalf, she returned to the optometrist and complained that the glasses caused her eyes to hurt and each time she was assured that the glasses would remedy her ailment when she became used to wearing them. On November 2 the plaintiff returned again to the optometrist and complained that she could not see out of one of her eyes. An examination by the optometrist disclosed that the sight of her right eye was completely gone and he then advised her to see a physician. The physician whom she consulted discovered that she was suffering from glaucoma, which had caused a detached retina of her right eye and which was at that time affecting her left eye. Subsequently her right eye was removed and her left eye treated in order to save it. She then brought suit against the corporation and the optometrist. Before the case was given to the jury, however, the case against the optometrist was dismissed and thereafter the trial court gave judgment for the defendant corporation. The plaintiff appealed to the Supreme Court of Alabama.

The first question discussed by the court was whether the relationship of master and servant existed between the corporation and the optometrist. When an optometrist undertakes to make an examination of the eyes, the court said, with a view of determining whether glasses will be of aid to his patient, he must exercise his professional or scientific skill, knowledge and judgment and he cannot be directed by an employer who has no such knowledge. But this does not mean that the employer, whose business the optometrist is conducting, is not answerable for the negligence of the optometrist resulting in injury to a third person, who has gone to the employer's place of business for an examination of her eyes and to be fitted with glasses. It was the defendant's business, under the control of its optometrist, it is true, but the defendant undertook for a pecuniary reward to render competent and proper optometric services. For all practical purposes, the defendant was engaged in rendering optometric service to the public. The defendant cannot, therefore, escape liability because of the independent character of the agent's or servant's business. The defendant was bound to see that those who sought examination of their eyes and the fitting of glasses received proper attention and service, and for any injury or damage to the defendant's customers, proximately caused by the want of skill or negligence of the optometrist, it, the defendant, is liable.

After reviewing several definitions of optometry, the court concluded that the optometrist in this case was not required, or even authorized, to diagnose and treat diseases of the eye. The optometry act of Alabama prohibits any optometrist from administering drugs in any form, from practicing, or claiming to practice, medicine or surgery in any sense, or from using any title or appellation intended or calculated to indicate the practice of medicine or surgery. Clearly, the court said, the duty resting on the optometrist was to examine the plaintiff's eyes for the "purpose of ascertaining any departure from normal (having reference to vision), measuring its functional powers, and adapting mechanical means for the aid thereof." If, however, in the performance of those duties, it would be apparent to a skilful optometrist that there existed in the eye a disease or malformation, the court inferred that it would be the optometrist's duty so to advise his patient in order that the proper medical or surgical treatment might be had. The evidence in this case, however, convinced the court that the disease of the plaintiff's eyes was not such a disease as should have been detected by a skilful optometrist. The corporation's optometrist, therefore, was not negligent in failing to detect it.

Since there was no breach of duty owed by the corporation to the plaintiff, the judgment for the defendant corporation was affirmed.—*Hampton v. Brackin's Jewelry & Optical Co., Inc. (Ala.), 186 So. 173.*

Privileged Communications: Wife of Physician Who Acts as Assistant Within Rule.—Where a statute, said the criminal court of appeals of Oklahoma, provides that a physician or surgeon shall be incompetent to testify as to any communication made to him by his patients with reference to any physical or supposed physical disease, or any knowledge obtained by a personal examination of any such patient, the same rule applies to the wife of the physician or surgeon who is his assistant in his office and by reason thereof hears the communication or sees the examination.—*Williams v. State (Okla.), 86 P. (2d) 1015.*

Society Proceedings

COMING MEETINGS

American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.

American Society of Anesthetists, Los Angeles, Dec. 14. Dr. Paul M. Wood, 745 Fifth Ave., New York, Secretary.

Annual Congress on Industrial Health, Chicago, Jan. 15-16. Dr. C. M. Peterson, 535 North Dearborn St., Chicago, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Pittsburgh, Jan. 5. Dr. John R. Simpson, Medical Arts Bldg., Pittsburgh, Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Kansas City, Mo., Jan. 19. Dr. Sam E. Roberts, Professional Bldg., Kansas City, Mo., Chairman.

Radiological Society of North America, Atlanta, Ga., Dec. 11-15. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.

Society for the Study of Asthma and Allied Conditions, Philadelphia, Dec. 9. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.

Society of American Bacteriologists, New Haven, Conn., Dec. 28-30. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.

Southern Section, American Laryngological, Rhinological and Otological Society, Columbia, S. C., Jan. 8-9. Dr. Walter J. Bristow, Doctors Bldg., Columbia, S. C., Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, Los Angeles, Jan. 26-27. Dr. Pierre Viole, 1930 Wilshire Blvd., Los Angeles, Chairman.

Western Surgical Association, Los Angeles, Dec. 15-16. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1929 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

18: 389-518 (Oct.) 1939

Formation and Movements of Lymph. C. K. Drinker, Boston.—p. 389.
Coronary Arteries of the Dog. M. B. Pianetto, Rosario, Argentina.—p. 403.
Hypertonic Glucose Solution in Angina Pectoris. D. Scherf and J. Weisberg, New York.—p. 411.
Deproteinated Pancreatic Extract (Depropanex): I. Effect in Treatment of Intermittent Claudication Due to Arteriosclerosis Obliterans. M. M. Fisher, A. W. Duryee and I. S. Wright, New York.—p. 425.
*Activities Associated with Onset of Acute Coronary Artery Occlusion. A. M. Master, S. Dack and H. L. Jaffe, New York.—p. 434.
Convallan in Cardiac Therapy. R. H. Major and L. H. Leger, Kansas City, Kan.—p. 444.
Capillary Rupture with Intimal Hemorrhage as Cause of Pulmonary Thrombosis. J. C. Paterson, Ottawa, Ontario, Canada.—p. 451.
Electrocardiographic Changes Associated with Experimental Alterations in Blood Potassium in Cats. F. L. Chamberlain, J. Scudder and R. L. Zwemer, New York.—p. 458.
Ruptured Popliteal Aneurysm: Report of Four Cases. W. M. Yater, Washington, D. C.—p. 471.
Loud, Musical, Diastolic Murmurs of Aortic Insufficiency: Clinical and Pathologic Observations on Their Cause and Mechanism of Their Production. Ballet, B. Gouley, C. F. Nichols and T. M. McMillan, Philadelphia.—p. 483.

Activities Associated with Onset of Coronary Occlusion.—In this paper Master and his associates offer evidence that occlusion of the coronary artery occurs irrespective of physical activity. They analyzed 1,440 attacks of coronary artery occlusion from the standpoint of the patients' activities preceding the attacks, the time of day when the attacks occurred, the patients' occupations and other associated factors. The distribution of occupations was approximately the same as that in the general population; therefore occupation and social status did not predispose to coronary occlusion. The circumstances preceding the onset of symptoms in 890 cases were sleep 22.3 per cent, rest 31.1 per cent, mild activity 20.2 per cent, moderate activity 8.5 per cent, walking 15.8 per cent and unusual exertion 2 per cent. Correlation of these percentages with the number of hours spent daily by the ordinary person in the same occupations indicated that the circumstances were coincidental and that none of them was causally related to the coronary occlusion. Thus coronary occlusion occurs irrespective of the state of physical activity of the body. Associated factors in 930 cases were meals 9.9 per cent, emotional excitement 5.6 per cent, surgical operation 6.6 per cent, infection 4.3 per cent and miscellaneous factors 1 per cent. It was concluded that, with the possible exception of surgical procedures, these factors did not play a role in the pathogenesis of coronary occlusion. Only two attacks of coronary occlusion were associated with trauma. Detailed histories of the activities and emotional state of patients for hours, days and weeks preceding attacks confirm the belief that physical activity and excitement are not factors in the onset of coronary occlusion. Sixty patients sustained an attack of coronary occlusion after having been bedridden for weeks or months. The time of onset was ascertained in 722 cases. Equal numbers occurred during the afternoon, evening and night and a slightly greater number during the morning. The attacks were distributed throughout all the hours of the day, with peaks at 2 a. m. and 10 p. m. This also indicates that activity is not a factor in the precipitation of coronary occlusion. Premonitory symptoms of the attack, such as pain in the chest, dyspnea or weakness were present in eighty of 170 cases. There is no evidence that physical effort or excitement produces intimal hemorrhage in the coronary arteries, which is the usual forerunner of thrombosis and occlusion. Intimal hemorrhage is the end result of the progressive, degenerative arteriosclerotic process and is probably a fortuitous event. It was found at necropsy as frequently in patients who had been bedridden prior to the occlusion as in those who were physically active.

American Journal of Pathology, Boston

15: 501-636 (Sept.) 1939

Occurrence of Virulent Tubercle Bacilli in Presumably Nontuberculous Lung Tissue. W. H. Feldman and A. H. Baggenstoss, Rochester, Minn.—p. 501.
Fixing and Staining Methods for Lead and Copper in Tissues. F. B. Mallory and F. Parker Jr., Boston.—p. 517.
Giant Cell Formation in Tonsils in Prodromal Stage of Chickenpox: Report of Case. T. H. Tomlinson Jr., Washington, D. C.—p. 523.
Traumatic Autotransplantation of Splenic Tissue. S. Jarcho and Dorothy H. Andersen, New York.—p. 527.
Comparison of Effects of Anterior Pituitary Hormone on Skeletal Tissues of Young and Mature Guinea Pigs. M. Silberberg and Ruth Silberberg, St. Louis.—p. 547.
Intracellular Bacilli in Intestinal and Mesenteric Lesions of Typhoid Fever. J. W. Adams Jr., Nashville, Tenn.—p. 561.
*Carcinoma of Lung: Analysis of Seventy-Four Autopsies. R. D'Aunoy, B. Pearson and B. Halpert, New Orleans.—p. 567.

Carcinoma of Lung.—D'Aunoy and his associates state that seventy-four cases of primary carcinoma of the lung were encountered in 6,623 necropsies on persons more than 1 year of age. Sixty-eight of the growths occurred in men and six in women. The age range was from 21 to 75 years. The average duration of illness was five months. One patient died in the third, four in the fourth, thirteen in the fifth, thirty-three in the sixth, nineteen in the seventh and four in the eighth decade of life. In almost half of the cases the primary growth was located in one or the other bronchus. Thirty-seven of the seventy-four carcinomas were composed of squamous cells, twenty-one of reserve cells and sixteen of columnar cells. The increasing importance of carcinoma of the lung as a clinical problem is emphasized by many recent publications. There is an apparently wide variance in the conceptions of individual authors as to the histogenesis and structure of carcinoma of the lung as no uniformity has yet been attained in classifying these growths. The difficulty may be superficial rather than essential. In the authors' opinion a classification on a histogenetic basis, combined with a nomenclature derived from the cell making up the growth, rather than from the structure which the cell forms, will go far toward simplifying the problem. The occasional overlapping of groups is not unexpected, since all carcinomas of the lung, they believe, are derived from a common ancestor cell, the reserve cell.

American Journal of Physiology, Baltimore

127: 415-604 (Oct.) 1939. Partial Index

Adrenalin Lactacidemia: Proportionality with Dose. F. R. Griffith Jr., Julia E. Lockwood and F. E. Emery, Buffalo.—p. 415.
Factors Affecting Toxicity of Potassium. A. W. Winkler, H. E. Hoff and P. K. Smith, New Haven, Conn.—p. 430.
Range and Variability of Blood Flow in Human Fingers and Vasomotor Regulation of Body Temperature. A. C. Burton, Philadelphia.—p. 437.
Radiating Power of Human Skin in Infra-Red. J. D. Hardy, New York.—p. 454.
Influence of Hypophysis on Carbohydrate Metabolism. S. Soskin, R. Levine and W. Lehmann, Chicago.—p. 463.
Motility of School Children During Sleep. G. Giddings, Emory University, Ga.—p. 480.
Influence of Air Movement on Heat Losses from Clothed Human Body. C.-E. A. Winslow, A. P. Gagge and L. P. Herrington, New Haven, Conn.—p. 505.
Effect of Subcutaneous Administration of Water and Certain Salts on Urine Volume. A. M. Walker, Philadelphia.—p. 541.
Role of Pituitary in Caloriogenic Action of Vitamin D. A. Bartoli, J. Feldman and C. I. Reed, Chicago.—p. 552.
*Effect of Posture on Peripheral Circulation. M. Nielsen, Copenhagen, Denmark; L. F. Herrington and C.-E. A. Winslow, New Haven, Conn.—p. 573.
Measurement of Insulin Action. D. R. Drury and P. O. Greeley, Los Angeles.—p. 581.

Effect of Posture on Peripheral Circulation.—Nielsen and his co-workers report that a passive change of body posture by a tilting from the horizontal to a feet down position (45 degrees from the horizontal) produces a peripheral vasoconstriction in subjects not adapted to warm environments. The degree of vasoconstriction increases with progressively warmer environments and higher angles of tilting. Higher angles of tilting or extremely hot environments are associated with a tendency to collapse. A rise of internal body temperature, roughly proportional to the degree of vasoconstriction, occurs in the vertical position and may be functionally associated with the stimulus to increased evaporation. The disturbance of the heat-regulatory function due to vasoconstriction in the tilted position is, to a certain degree, compensated by an increase in evaporation. Except under severe conditions, toe temperatures change in an opposite direction to general cutaneous temperatures, possibly involving a protective mechanism against local chilling.

American Journal of Surgery, New York

40: 1-218 (Oct.) 1939. Partial Index

Neoplasms of Cecum and Ascending Colon. F. H. Lahey, Boston.—p. 3.
Surgical Removal of Lesions Occurring in Sigmoid and Rectosigmoid. C. F. Dixon, Rochester, Minn.—p. 12.
Cancer of Rectum and Rectosigmoid: Diagnosis and Treatment. F. W. Rankin and A. S. Graham, Lexington, Ky.—p. 18.
Operability and Types of Surgery in Cancer of Rectum. T. E. Jones, Cleveland.—p. 45.
*Immunization of Peritoneum. F. A. Coller and S. Rife, Ann Arbor, Mich.—p. 61.
Water and Chemical Balance in Surgery of Colon. T. G. Orr, Kansas City, Kan.—p. 70.
Surgical Management of Chronic Intractable Ulcerative Colitis. H. W. Cave, New York.—p. 79.
Gastrojejunocolic Ulcer and Fistula. W. Walters and O. T. Clagett, Rochester, Minn.—p. 94.
Operability, Morbidity and Mortality Factors in Carcinoma of Colon. A. Ochsner and M. DeBakey, New Orleans.—p. 103.
Diagnostic Value of Sigmoidoscopy and Biopsy. F. C. Yeomans, New York.—p. 123.
Injuries of Colon: Review of Sixty-Two Cases in Negro Patients. F. K. Boland, Atlanta, Ga.—p. 126.
Lymphatic Distribution of Colon and Rectum. W. W. Looney, Dallas, Texas.—p. 143.
Treatment and Prognosis of Diverticulitis of Colon. P. W. Brown, Rochester, Minn.—p. 162.
*Malignant Disease of Colon: Factors Influencing Operability, Morbidity and Mortality. A. W. Allen and C. E. Welch, Boston.—p. 171.
Experiences with Resection of Colon and Elimination of Colostomy. W. W. Babcock, Philadelphia.—p. 186.
Multiple Polyposis: Congenital, Heredofamilial, Malignant. D. C. McKenney, Buffalo.—p. 204.

Immunization of Peritoneum.—Coller and Rife point out that during the last ten years three immunizing agents have been employed extensively for immunization of the peritoneum. These are (1) the vaccine developed by Steinberg and Goldblatt, (2) the vaccine prepared by Bargen and (3) the amniotic fluid preparations originally suggested by Johnson. Such factors as the species of laboratory animal used, the type and dose of immunizing substance employed and the time and mode of its administration make it difficult to compare the observations of one investigator with those of another. It is logical to assume that the peritoneum of one animal will not react in the same manner as that of another, and the peritoneums of animals will all differ in some respects from that of man. As yet no adequate control series has been reported. From a clinical point of view, the newer concept of the protective value of the exudate in peritonitis has a practical value. In operations done on patients with peritonitis it would seem harmful to carry out manipulations designed to wipe or wash away exudate that is part of a protective mechanism against the infection. If free exudate is removed it must be done in the gentlest fashion, by careful aspiration. The authors can see no reason for the routine use of any of the substances suggested to increase the immunity of the peritoneum. If patients are properly prepared for operation and if the operation is carried out with careful meticulous technic, peritonitis rarely supervenes. Some substance that will produce rapid local leukocytosis is of value in those instances in which, because of accident of operation or disease, the large intestine is opened. The authors' experience in these circumstances has been most satisfactory with colibactragen (Steinberg). They feel that it has a distinct value when used in the stage of contamination and that it has little or no value once the infection is established. Postoperative peritonitis in cases previously without infection is usually due to errors of operative technic that cannot be corrected by the introduction into the peritoneum of anything except better surgical technic.

Malignant Disease of Colon.—Allen and Welch reviewed 634 patients with cancer of the colon admitted to the Massachusetts General Hospital from 1925 to 1938 inclusive. Of these, in 365 the colon was resectable. This operability can be increased only by earlier diagnosis and by abandonment of the idea that the disease is incurable or that the patient cannot stand the operation. Many times help is denied until obstruction sets in or the patient becomes moribund from perforation or hopeless extension of the disease. In considering the various locations of cancer of the colon and the operative procedures giving the most satisfactory outcome, the authors state that each surgeon must adopt the method that gives him the best result. Gross contamination of the peritoneal cavity must be avoided. The diseased area must be removed and, in most instances, continuity of the intestine reestablished. The blood supply to the anastomosed ends must be preserved. Sutures must approximate the serous coats of the intestine, and the mucous membrane must be inverted. There must be no tension on the suture line and no drains resting near it. Traps in the mesentery must be closed and raw surfaces peritonized when possible. Proximal complementary decompression must be established if not provided by a previous procedure. If to these rules good general surgical principles are added the results will be satisfactory. The authors have found that two stage procedures have lowered their mortality. They believe preliminary proximal operations should be done routinely for malignant lesions of the large intestine whether obstruction does or does not exist, and regardless of the age or condition of the patient. Too many "good risk" patients have succumbed to one stage operations on the intestine. The hospital stay of the patient operated on in two stages for cancer of the colon is increased on an average of ten days, but the fatal complications of peritonitis and pneumonia are materially reduced. The mortality from radical operation was approximately 20 per cent in one stage procedures as compared with 13 per cent in the two stage operations.

Archives of Neurology and Psychiatry, Chicago

42: 789-978 (Nov.) 1939

Involvement of Nervous System Associated with Endocarditis: Neuropsychiatric and Neuropathologic Observations in Forty-Two Cases of Fatal Outcome. J. W. Kernohan, H. W. Woltman and Arlie R. Barnes, Rochester, Minn.—p. 789.
Subdural Shadows in Pneumoencephalograms: Their Diagnosis, Origin and Significance. T. J. C. Von Storch and A. Buermann, Boston.—p. 810.
Effect of Epinephrine on Convulsions. E. Gellhorn, C. W. Darrow and L. Yesinick, Chicago.—p. 826.
*Role of Allergy in Multiple Sclerosis: Incidence of Atopy in Series of Forty Cases. R. L. Baer and M. B. Sulzberger, New York.—p. 837.
Gross Pathology of Oligodendrogliomas. K. Löwenberg and R. W. Waggoner, Ann Arbor, Mich.—p. 842.
Rhythmic Variation of Respiratory Excursion with Bilateral Injury of Cortical Efferent Fibers. R. V. Grimmer, F. H. Hesser and O. R. Langworthy, Baltimore.—p. 862.
Human Pyramidal Tract: Fiber and Numerical Analysis. A. M. Lassek and G. L. Rasmussen, Charleston, S. C.—p. 872.
*Follow-Up Study of Five Hundred Patients with Schizophrenia Admitted to Hospital from 1913 to 1923. T. A. C. Rennie, with the help of J. B. Fowler, Baltimore.—p. 877.
Pinealoma of Diffuse Ependymal Origin. R. P. Mackay, Chicago.—p. 892.
Hemorrhages into Central Nervous System Following Lumbar Spinal Puncture. S. Androp, Catonsville, Md.—p. 903.
Classroom Outline for Pathologic Diagnosis of Primary Intracranial Neoplasms: Six Differential Characteristics. L. Alexander, Boston.—p. 912.

Allergy in Multiple Sclerosis.—Baer and Sulzberger undertook to study patients with multiple sclerosis in order to determine how many had an atopic hypersensitivity. This type of allergy, which is clinically represented by asthma, hay fever and atopic dermatitis, is characterized chiefly by (1) a high incidence of atopic conditions in the familial as well as in the personal history, (2) wheal responses to scratch and intradermal tests with the protein fractions of foods, inhalants and other materials, (3) eosinophilia in the blood and (4) frequent observation of passive transfer antibodies or reagins (Prausnitz-Küstner reaction). Atopy is only one of many characteristic forms of allergy known to appear in man (others are, for example, contact allergy, tuberculin allergy and various forms of drug allergy). The authors made their studies on forty patients with multiple sclerosis. On all forty patients, scratch tests were made with from sixty-four to seventy common food allergens and with thirty-four common inhalant and other allergens. Histories of thirty of the forty patients were taken with regard to the familial and personal incidence of atopic conditions, the ingestion of drugs and exposure to occupational as well as other environmental substances prior to the onset of the disease. From the remaining ten patients no exact histories could be obtained. Of the thirty patients with multiple sclerosis who were completely studied, ten, or 33 per cent, presented evidence of personal or familial atopic disease or positive wheal reactions to skin tests or both. When these figures are compared with those in the literature relating to the incidence of atopy in an unselected population, it will be seen that these results correspond with the high average values submitted by investigators who have performed similar studies on unselected groups. The authors conclude therefore that, with the criteria and methods described and with allowance for the factor of error present in a series of this small size, their results in the forty cases of multiple sclerosis do not demonstrate a significant increase over the normal incidence of atopy. This statement does not, of course,

exclude the possibility that in an occasional instance multiple sclerosis-like symptoms may be caused by an atopic mechanism. Nor do these results in any way preclude the possibility that some nonatopic form of allergy may play a role in multiple sclerosis.

Follow-Up Study of Patients with Schizophrenia.—Rennie studied 500 patients exhibiting a typical picture of parergastic disorder, commonly designated as schizophrenia or dementia praecox. This group is made up of the patients admitted between May 1913 and May 1923. Of the 500 cases selected for the study, the author has been unable to get adequate facts in only forty-four. Concerning 456 patients he has some statement of the course of the disease, ranging from one to twenty-six years after hospitalization. The method of follow-up study employed was to trace the patient's present status by the use of a letter of inquiry to the patient, relatives or family physician; a personal interview by a staff member, or an interview with the patient or family by a social worker employed for this project. A number of patients were followed by all three methods. In discussing the results of this investigation, the author says that at the time of discharge from the clinic 42.7 per cent were well or improved, whereas 57.3 per cent left the hospital unimproved. The course of the illness seems more favorable for women than for men. At the end of twenty years the picture is less favorable than at the end of nine years or at the time of discharge. After twenty years, 27 per cent of the patients show recovery; an additional 13 per cent give evidence of some productivity. There is great variability in the course of the disorder as regards rehospitalization; 33.5 per cent of the total series of patients were never able to leave a hospital; 32.6 per cent were never readmitted to any hospital. While rehospitalization is frequent, this does not necessarily affect the final outcome. For the majority of the patients who recover a single brief period of hospitalization is the rule. There are exceptions to this, in that one fourth of the total number had a period of readmission to a hospital. One patient, after ten years of psychotic behavior in a hospital, appears to have been completely recovered for eight years. Another patient, after eight years of hospitalization, appears to have been completely recovered for fourteen years. In a few other cases there have been as many as five hospitalizations before recovery was effected. Thus, a second or even a third or fourth hospitalization does not necessarily spell poor prognosis. Nonetheless, it is striking that the period of hospitalization for the recovered group is for the most part less than a year. In marked contrast to the relatively brief period of hospitalization and to the single admission of the majority of the recovered patients are the observations on the group of permanently hospitalized patients. For the most part these persons show a protracted and uninterrupted period of hospitalization. However, gaps of time between the first and the permanent hospitalization occur with 35 per cent of the group. Permanent recovery is difficult to predict, even after long years of apparent well-being. These observations tend to reemphasize the fact that extreme caution must be exercised in offering prognosis in cases of schizophrenia.

Archives of Pathology, Chicago

28: 427-612 (Oct.) 1939

Transposition of Great Cardiac Vessels, with Special Reference to Phylogenetic Theory of Spitzer. J. S. Harris, Durham, N. C., and S. Farber, Boston.—p. 427.
*Vitamin C Deficiency and Intestinal Fusospirochetosis. F. M. Woolsey and J. R. Black, Durham, N. C.—p. 503.
Organic Lesions Produced by Polyvinyl Alcohol in Rats and Rabbits: Toxicopathologic Investigation of Experimental Thesaurosis. W. C. Hueper, New York.—p. 510.
Cultivation of Viruses: Critical Review. M. Sanders, New York.—p. 541.

Ascorbic Acid Deficiency and Intestinal Fusospirochetosis.—According to Woolsey and Black, a microscopic study of sections of intestines obtained at necropsy in twenty-four cases of intestinal disease (including diphtheritic and ulcerative colitis, typhoid, dysentery due to Flexner's bacillus and enteritis due to Giardia and Ascaris) revealed fusiform bacilli in twelve instances. In only two of these were Levaditi stains available, and in these spirochetes were seen. In all but two of the twelve cases in which fusiform bacilli were found there were infections which could have caused a break in the intestinal mucosa. All of these patients had been on a diet deficient in ascorbic acid. This type of diet lowers the resistance of the intestines to infections. The manner in which this resistance is lowered is probably complex, but the authors' experiments on animals receiving a diet deficient in ascorbic acid showed numerous small hemorrhages in the intestines, indicating that at times these hemorrhages are sufficiently profuse to cause necrosis and thus a break in the mucosa which allows the organisms present to gain a foothold. What part this mechanism plays in clinical cases is difficult to evaluate. The evidence of other causes at necropsy does not preclude the possibility that some agent other than the ascorbic acid deficiency may have been present before the fusospirochetal infection. However, the work of Koch indicates that extreme ascorbic acid deficiency leads to definite intestinal lesions with fusospirochetes present. When a break in the mucosa of the intestines is caused by parasites, bacteria or a deficiency of ascorbic acid fusospirochetal organisms, if present, may cause further damage. However, at present there is no indication that the intestines can be damaged by fusospirochetes without the aid of some other factor.

Canadian Medical Association Journal, Montreal

41: 323-428 (Oct.) 1939. Partial Index

Disseminated Blastomycosis: Case. L. J. Solway, M. Kohan and H. G. Pritzker, Toronto.—p. 331.
A Mold from the Ear. Eleanor Silver Dowding and M. R. Levey, Edmonton, Alta.—p. 336.
Renal Hypoplasia with Pyelitis Cystica and Ureteritis Cystica. D. W. MacKenzie and H. J. Tweddell, Montreal.—p. 345.
Iodine Deficiency in Relation to Stillbirth Problem. W. N. Kemp, Hampstead, Que.—p. 356.
Lobar Pneumonia. L. C. Montgomery and S. L. Richardson, Montreal.—p. 362.
Diagnosis and Treatment of Neurotic Disorders. E. P. Lewis and D. G. McKerracher, Toronto.—p. 366.
Treatment of Severe Cases and Complications of Varicose Veins in Legs. I. D. Kitchen, Toronto.—p. 374.
Peripheral Vascular Complications in Prostatic Surgery. A. Strasberg, Montreal.—p. 377.
Artificial Pneumothorax (Five Year Report). S. J. Hawkins and E. N. Coutts, Kitchener, Ont.—p. 379.
Prenatal Care (Eleven Year Study of Dalhousie University Public Health Centre Prenatal Clinic). A. L. McLean and W. G. Colwell, Halifax, N. S.—p. 382.

Endocrinology, Los Angeles

25: 491-660 (Oct.) 1939. Partial Index

*Studies of Metabolism of Androgens in Women. E. C. Hamblen, R. A. Ross, W. K. Cuyler, Margaret Baptist and Catherine Ashley, Durham, N. C.—p. 491.
*Comparative Study of Effects of Male and Female Sex Hormones on Human Vaginal Smear. N. O. Rothermich, Columbus, Ohio.—p. 520.
Efficiency of Extraction and Separation of Certain Anterior Pituitary Hormones. A. J. Bergman, O. B. Houchin and C. W. Turner, Columbia, Mo.—p. 547.
Diethylstilbestrol Compared to Estrone in Causing Estrus in Spayed Mice; and in Conjunction with Progestin in Inducing Sexual Receptivity in Spayed Guinea Pigs. J. A. Leighty and H. J. Wiek, Indianapolis.—p. 597.
Inactivation of Endogenous Estrogen by Liver. N. B. Talbot, Cambridge and Boston, Mass.—p. 601.
Role of Pituitary Stalk in Regulation of Anterior Pituitary, with Special Reference to Thyrotropic Hormone. U. U. Uotila, Boston.—p. 605.
Effect of Adaptation to Various Damaging Agents on Female Sex Organs in Rat. H. Selye, Montreal.—p. 615.
Part Played by Age and Female Sex Hormones in Resistance to Infection. D. H. Sprunt, Durham, N. C.—p. 625.
Effects of Proteolytic Enzymes on Purified Gonadotropic Hormones. A. A. Abramowitz and F. L. Hisaw, Cambridge, Mass.—p. 633.

Metabolism of Androgens in Women.—Hamblen and his colleagues determined the urinary androgens, by a modification of the colorimetric method of Oesting, in a group of twenty-seven women with various levels of ovarian function. In all, 672 twenty-four hour specimens of urine were titrated. Daily titers of the same woman varied markedly. Normal androgenic titers were obtained in five healthy women, aged 21 to 43 years, who experienced cyclic menses; in two women who had had operations involving hysterectomy with ovarian conservation and in five women who had had operations involving hysterectomy and bilateral oophorectomy; in two women, 14½ and 19 years of age, with belated menarches who were staturally and sexually retarded, and in two women, aged 17 and 29 years, who had functional menometrorrhagia associated with various degrees of endometrial proliferation and differentiation. Androgenic titers tended to be high in four women, from 16 to 30 years of age, who had had episodes of amenorrhea, which ranged in duration from four months to five years, and in five women, from 42 to 74 years of age, whose last episodes of uterine bleeding had occurred from nine months to twenty-six years before the

present observation. Injections of testosterone propionate, which varied as to single doses from 10 to 100 mg. and as to number from one to ten, resulted in definite elevations of androgenic titers. The recoveries of the androgen injected ranged from 7.6 to 71 per cent. Intensive estrogenic therapy of two patients caused definite decreases in androgenic titers. From the data reported it is suggested that the chief source of androgens in women is not the ovaries but most likely the adrenals. The complexional coloring and the androgenic titers of women apparently are related. The increased androgenic titers of some women who have periods of amenorrhea may be of diagnostic, prognostic and therapeutic import. An apparently increased production of androgens during the early postmenopausal period may signify the existence of another mechanism for stabilization of pituitary function after ovarian effects have become minimal. The androgens may play an active part in the production of the regressive alterations in the aging sexual system of women.

Effects of Endocrines on Vaginal Smear.—Rothermich endeavored to demonstrate what effect, if any, androgen has on the human vagina as revealed by the vaginal smear. Eleven menopausal women receiving estrogen responded with the typical follicular smear. In eleven similar women treated with testosterone the vaginal smear, if atrophic beforehand, showed no change; if previously follicular in character, the smear regressed to the atrophic type, in which state it persisted. The stimulative effect of estrogen could be entirely nullified by the simultaneous administration of adequate amounts of testosterone. The following conclusions seem indicated: Androgen has no direct stimulating action on the human vagina. Androgen nullifies, counteracts or neutralizes the usual action of estrogen on the human vagina.

Journal of Bone and Joint Surgery, Boston

21: 839-1112 (Oct.) 1939. Partial Index

Resection of Radial Head and Neck: End-Result Study of Thirteen Cases. B. B. King, New York.—p. 839.
Methods Used in Handling Epidemic of Poliomyelitis in Ontario in 1937. A. B. LeMesurier, Toronto.—p. 867.
Etiology of Spondylolisthesis. M. Batts Jr., Ann Arbor, Mich.—p. 879.
*Use of Insulin as Adjunct in Treatment of Bone and Joint Tuberculosis. R. L. Nichols, Minneapolis, and E. L. Compere, Chicago.—p. 885.
Treatment of Ununited Fractures of Carpal Navicular. J. M. Edelstein, Johannesburg, South Africa.—p. 902.
Recurrence of Flexion and Adduction Deformities Following Operative Fusion of Hip and Subtrochanteric Osteotomy. F. H. Downing, Fresno, Calif.—p. 909.
Functioning False Shoulder Joint Following an Old Dislocation. K. Christophe, Boston.—p. 916.
Tendon Transplantation: End-Result Study of 458 Transplantations. A. R. Carpenter, Binghamton, N. Y.—p. 921.
Diagnosis and Treatment of Athetosis and Dystonia. T. J. Putnam, New York.—p. 948.
Recurrent Luxation of Ulnar Nerve by Congenital Posterior Position of Medial Epicondyle of Humerus. M. S. Burman and C. J. Sutro, New York.—p. 958.
Operation for Correction of Hammer Toe. P. W. Lapidus, New York.—p. 977.
*Orthopedic Treatment of Strümpell-Marie Arthritis. L. T. Swaim, Boston.—p. 983.
Amputation of Foot, with Calcaneotibial Arthrodesis. H. B. Boyd, Memphis, Tenn.—p. 997.
*Epiphysitis of Os Calcis. H. E. Simon and B. Williamson, Birmingham, Ala.—p. 1015.
Fractures of Carpal Navicular: Importance of Special Roentgenography. A. S. Rothberg, New York.—p. 1020.
Coxa Plana: Report of Two Bilateral Cases in Brothers. W. H. Hagen, East Orange, N. J.—p. 1028.

Insulin in Treatment of Bone and Joint Tuberculosis.—Because some children suffering from bone and joint tuberculosis cared for in a convalescent home affiliated with the University of Chicago failed to gain in weight insulin therapy was recommended. Nichols and Compere selected fourteen patients with tuberculosis and one with bilateral Legg-Perthes disease, from 3 to 13 years of age, for this adjunct therapy. To each of these patients from 2 to 5 units of insulin was administered twenty minutes before each meal. In each instance the patient manifested more interest in his food. For the first time, some complained that they were hungry. Twelve of the fifteen patients gained from 1 to 3 pounds (0.45 to 1.36 Kg.) in weight. In three of the twelve cases there was no consistent gain in weight until after the injections had been discontinued. There was a simultaneous improvement in the general appearance and well-being of the patients. The authors are not able to postulate conclusions from so few cases. It seems to them that injection of insulin is not indicated as a routine procedure in the treatment of bone and joint tuberculosis except for patients who are finicky eaters and who, under the best of environmental conditions, fail to gain or actually lose weight.

Orthopedic Treatment of Strümpell-Marie Arthritis.—Swaim reports his results in 106 cases of Strümpell-Marie arthritis observed over twenty-two years. The sacro-iliac joints were fused early in all of the 106 cases. After fusion was complete, the disease stopped. In some cases the hips became fused also. The author's theory has been that ossification represents the result of nature's method of permanent immobilization of the spine to prevent strain and motion and inflammation in the ligaments. Therefore he believes that orthopedic treatment should begin at least within the first three years, although much can be done within nine years. Prior to 1930, forty-five patients had been treated by orthopedic measures in an attempt to prevent the usual deformity of rounded thoracic spine, flat upper part of the chest and buckled body, with protruding head and sometimes with fused hips. The method of correcting posture was as follows: The patient was kept recumbent, and the spine was gradually hyperextended in bed, first by removing the pillows under his head until he was either flat or as straight as possible; second by using plaster half-shells to support and to stretch the spine. Relaxing hot fomentations were applied to the whole spine twice daily for twenty minutes, and corrective exercises to straighten the body and to expand the chest were taught and supervised morning and evening. When the back was as straight as it seemed possible to make it, steel braces which drew the shoulders back were fitted, or short spring braces with elastic shoulder straps were tried; even corsets were used at times to reinforce the braces. Thirty-five of the forty-five patients had completely fused spines, and thirty-one had poor posture in spite of treatment. The results were so unsatisfactory from a postural standpoint that a better method of preventing deformity had to be devised; plaster jackets were tried. It was found that after the patient was completely immobilized in a jacket for several months, motion in the spine was increased rather than lost by the fixation. With the exception of the use of the jacket, no change was made in the previous treatment. If the spine was not straightened by the end of two weeks a jacket was applied and was renewed at regular intervals. The jacket was kept on uninterruptedly for several weeks, until there was no spasm. Then only were new jackets made. Plaster jackets were renewed until the best possible correction was obtained; then a more permanent leather jacket (steeled in back and laced in front) was made on a plaster model. It was cut high in front and low in back and, being waxed, was designed to last for several years. In most cases it was worn day and night. After each plaster jacket was hard a greater lordosis was attempted. Walking was encouraged as the adductor spasm disappeared. The results were encouraging. The spasm and pain disappeared during the first few days, and the general condition improved with the lessened pain and better nights of rest. From the patients' standpoint, the jackets have given the greatest relief to the hips, ribs and neck. From the orthopedic point of view, postural deformity has not occurred, chest expansion has increased and the general health has been better. Sixty-two patients have worn the leather jackets. All became symptomatically better. They were made more comfortable, except three who were uncooperative. All have preferred to wear their jackets rather than to go without them. Conclusions about the physical effects are drawn from twenty-three patients who have worn jackets for from four to nine years. Good posture was maintained in five, improved in fifteen and lost in three; one of these refused the jacket after two years, one cut his jacket in front so that it no longer gave any support and one was uncooperative. No new hip trouble developed in any of the sixty-two cases. Seven of the eleven patients with hip symptoms who wore their jackets from four to nine years became completely symptomless, three patients with fused hips showed no change and one patient was unaccountably worse. Chest expansion decreased in seven cases, was unchanged in two and increased in fourteen. Weight increased in twenty cases, remained the same in two and decreased in one. Sixteen patients are working, six are at home (unemployed but looking for work), and one died of carcinoma of the breast. The study definitely suggests that ossification is much less rapid in patients treated with jackets. The results for such patients were superior to those for the forty-five previously treated without jackets.

V 19

Epiphysitis of Os Calcis.—Simon and Williamson warn that in children, particularly in boys, between 7½ and 17 years of age the occurrence of painful heels should suggest the possibility of epiphysitis of the os calcis. The characteristic x-ray observations are fragmentation, rarefaction, narrowing and irregularity in outline of the epiphysis, with later excessive calcification. The condition is self limiting, and recovery occurs spontaneously when the epiphyses unite at about 17 years of age. The etiology has not been definitely established, but the role of trauma seems to be of some significance. Trauma, infection, nutritional disturbances, developmental abnormalities, disturbances in innervation and endocrine imbalance have all been blamed for the condition. It is possible that a combination of several of these factors is sometimes responsible. It is also logical to assume that the cause is not the same in every case. The wearing of sandals, rubber-soled shoes or no shoes at all has been a rather constant observation.

Journal of Infectious Diseases, Chicago

65: 97-224 (Sept.-Oct.) 1939. Partial Index

Effect of Sulfanilamide on Shwartzman Phenomenon and on Growth of Meningococci in Vitro. S. S. Schneierson, New York.—p. 97.
Ecto-Enzyme of Clostridium Welchii Which Decomposes Blood Group Specific Substance A. F. Schiff, New York.—p. 127.
Occurrence of Several Unusual Types of Salmonella in Human Infections. F. Schiff and Lotte Strauss, New York.—p. 160.
Nicotinamide and Related Compounds as Essential Growth Substances for Dysentery Bacilli. A. Dorfman, S. A. Koser, H. R. Reames, K. F. Swingle and F. Saunders, Chicago.—p. 163.
Effect of Alcohol on Chemotactic Response of Leukocytes. R. G. Kleper and W. J. Nungester, Ann Arbor, Mich.—p. 196.
*Agglutinins for Bacterium Necrophorum in Serum of Patients with Chronic Ulcerative Colitis. G. M. Dack, J. B. Kirsner, L. R. Dragstedt and R. Johnson, Chicago.—p. 200.
Intraneural Injections of Serum as Barrier to Migration of Virus in Experimental Poliomyelitis. J. A. Harrison and O. C. Woolpert, Chicago.—p. 214.
Bacillary Dysentery Developing in Monkeys on "Vitamin M" Deficient Diet. Martha Janota and G. M. Dack, Chicago.—p. 219.

Bacterium Necrophorum Agglutinins in Serum of Colitis Patients.—Dack and his co-workers collected seventy-six specimens of serum from thirty-six patients in different stages of chronic ulcerative colitis. There was a definite correlation of the appearance of Bacterium necrophorum with the agglutinins for this organism and with the severity of the disease. The severer the disease the greater the ease of isolation of the bacterium and demonstration of necrophorum agglutinins. The inability to find the organism in certain cases may not mean its absence but may represent the technical difficulties encountered in this work. In three patients with chronic ulcerative colitis there were homologous antigens for this serum. In one of these patients the serum reacted only with the homologous strain. In patients with lesions of the colon other than chronic ulcerative colitis agglutinins for one or more of the six antigens studied were found, in some instances in appreciable amount. In general agglutinins were found in higher titer in patients with ulcerating carcinomas of the rectum than in patients with minor lesions of the colon. In thirty-six patients in which the colon appeared normal on proctoscopic examination, Bacterium necrophorum was not found and agglutinins for three of the antigens were absent from the serum.

Journal of Investigative Dermatology, Baltimore

2: 231-300 (Oct.) 1939

Measurement of Hydrogen Ion Concentration of Skin Surface: III. Measurements on Arms of Children with No Apparent Skin Lesions. I. H. Blank, Boston.—p. 231.
Id.: IV. Daily Variations for Adult Females with No Apparent Skin Lesions. I. H. Blank, Boston.—p. 235.
Histology of Intracutaneous Tuberculin Reaction in Human Skin. H. C. Hinshaw and W. H. Feldman, Rochester, Minn.—p. 243.
*Tobacco Skin Reactions and Their Clinical Significance. J. Harkavy, New York.—p. 257.
Effect of Fever Artificially Induced on Skin Sensitivity of Guinea Pigs to Turpentine. L. Goldman, Cincinnati.—p. 281.
Mitotic Rhythm in Human Epidermis: Introduction and Review of Literature. Zola K. Cooper, St. Louis.—p. 289.

Cutaneous Reactions to Tobacco.—The incidence of cutaneous reactions to tobacco was studied by Harkavy in (1) 400 normal smokers, male and female, (2) 126 adult female nonsmokers, (3) 319 control smokers consisting of forty-seven normal persons and 292 adult patients suffering from various ailments, (4) 140 patients with thrombo-angiitis obliterans, (5) thirty-one patients with peripheral vascular disease associated with arteriosclerosis and (6) 100 patients with coronary disease and angina pectoris. These studies indicate that positive cutaneous reactions to tobacco (prepared according to a method that the author describes) represent a true immunologic response. This was demonstrated by (1) the presence of tobacco reagins in patients reacting positively, (2) specific absorption of these reagins by corresponding tobacco allergens in patients with multiple sensitization and (3) the induction of a characteristic local eosinophilic reaction in the immediate urticarial response in patients with thrombo-angiitis obliterans, coronary artery disease and migrating phlebitis tested intradermally with tobacco. This is further attested experimentally, in that in about 33 per cent of male rats given daily injections by the intraperitoneal route, with the same tobaccos employed in testing the patients, gangrene of the toes developed. These animals were shown to be sensitized to tobacco by the Schultz-Dale technic. Of the 140 patients with thrombo-angiitis obliterans tested with ragweed and timothy pollen, horse dander and tobacco 68 per cent gave positive reactions to tobacco only of 1 plus and over, and 44 per cent of these had reagins for tobacco. An additional 10 per cent gave plus-minus reactions, making a total of 78 per cent, the patients with thrombo-angiitis obliterans cases reacting to tobacco only. This is in contrast to 9 per cent of reactions to tobacco only in the 400 normal control smokers. Twelve patients with thrombo-angiitis obliterans tested with nicotine tartrate 1:10,000 and 1:5,000 gave completely negative reactions. Of the 100 patients with coronary artery disease and angina pectoris 44 per cent reacted to tobacco and ten of fourteen had reagins to tobacco. The author infers from these observations that tobacco allergy plays an important part in certain forms of vascular disease as well as in symptoms referable to other systems such as the respiratory, gastrointestinal and cutaneous. The positive reactions assume etiologic significance since they can be correlated with the fact that in the patients studied, particularly in those with thrombo-angiitis obliterans or angina pectoris with or without coronary artery disease, discontinuance of smoking causes an arrest in the progress of the disease and resumption calls forth an exacerbation of all symptoms. Although it has been impossible to adduce any demonstrable proof of sensitization to nicotine as such, the question of hypersensitiveness to its alkaloid on theoretic grounds cannot be dismissed completely. Sensitiveness to drugs and chemicals may exist irrespective of cutaneous reactions. Aside from its possible sensitizing effect, the pharmacologic action of nicotine in all probability plays an accessory part through its constrictive influence on blood vessels with a consequent diminution in blood flow in the tissues involved. Such a result, common in all smokers, is, however, transitory in normal persons. In itself it evokes no notable symptoms, but it may become of utmost importance in the evolution of pathologic tissue changes in persons allergic to tobacco. In the latter, tobacco hypersensitiveness may possibly intensify the pharmacologic action of nicotine. The immunologic and clinical evidence presented suggests that tobacco has an inciting role in thrombo-angiitis obliterans and in certain types of coronary artery involvement.

Journal of Urology, Baltimore

42: 481-650 (Oct.) 1939. Partial Index

Affections and Lesions of Prostatic Urethra. E. G. Ballenger, Atlanta, Ga.—p. 481.
Diagnosis and Treatment of Secondary Anaerobic Infections of Kidney Wounds. C. P. Mathé, San Francisco.—p. 488.
Closure of Loin Wound Without Drainage After Nephrectomy for Tuberculosis. E. L. Keyes, New York.—p. 496.
Massive Hydronephrosis Complicated by Hydro-Ureter: Report of Three Cases. W. C. Stirling, Washington, D. C.—p. 520.
*Super Voltage Radiation in Treatment of Bladder Tumors. F. H. Colby, Boston.—p. 538.
Anatomic Origin of Benign Prostatic Enlargement. C. L. Deming and J. S. Wolf, New Haven, Conn.—p. 566.
Obstruction in Neck of Bladder: Criteria of Operability. H. C. Habein, Rochester, Minn.—p. 581.
*Clinical Significance of Increased Serum "Acid" Phosphatase in Patients with Bone Metastases Secondary to Prostatic Carcinoma. J. N. Robinson, Ethel Benedict Gutman and A. B. Gutman, New York.—p. 602.
Effect of Testosterone on Kidney. H. Selye, Montreal.—p. 637.
Methods of Anesthesia for Transurethral Prostatic Resection and Other Cystoscopic Procedures. E. B. Tuohy and G. J. Thompson, Rochester, Minn.—p. 642.

Radiation for Bladder Tumors.—Colby used the million volt x-ray generator in the treatment of eight malignant bladder tumors. Favorable effects from its use, as with other forms of high voltage therapy, in causing tumor regression have been

evident. Likewise, disappointments have been encountered in other tumors, which seem to be "radioresistant." Patients seem to tolerate this high voltage and short wavelength, showing less general reaction, x-ray sickness and cutaneous change than with lower voltages. Screening sufficient to cut out the rays delivered by the 200 kilovolt machine eliminates the destructive effect of the longer waves, so that larger doses with deeper penetration are employed without untoward results. The author considers wide surgical excision the most suitable treatment for malignant tumors of the bladder, and when possible circumscribed growths are removed by operation. He advises supervoltage radiation only when the extent of the tumor renders operation impracticable or other factors make surgical intervention unwise. Usually debilitated patients with extensive disease are irradiated. Although his series is entirely too small for a fair evaluation of this form of treatment he states that certain tumors appear profoundly affected, with considerable regression. Those portions of the tumor which project into the bladder cavity seem to be affected considerably more than those which have extended through the wall of the bladder. Other tumors are affected little, if at all, and are considered "radioresistant." The dosage so far employed is probably considerably less than that which is possible, but more experience is necessary to standardize dosage and determine its ultimate effect.

Increased Serum "Acid" Phosphatase in Carcinoma.—From their experience and from the reports in the literature (forty-four cases in all), Robinson and his colleagues conclude that increased serum "acid" phosphatase activity is consistent and specific enough in occurrence to be helpful in the differential diagnosis of prostatic carcinoma with skeletal metastases. The determination of serum "acid" phosphatase activity appears to be a useful supplement to the clinical and x-ray study of patients with prostatic carcinoma, particularly if surgical procedures are contemplated. The presence of increased serum "acid" phosphatase activity in patients with prostatic carcinoma implies dissemination of the primary tumor and in this sense has an unfavorable significance; an upward trend in serum "acid" phosphatase values may signify further metastatic involvement. The serum phosphatase activity in sixteen of the nineteen cases of prostatic carcinoma with skeletal metastases that they examined was found to exceed 3 units per hundred cubic centimeters. In thirteen cases of prostatic carcinoma without x-ray evidence of metastases to bone and in six cases of benign prostatic hypertrophy the values were within normal limits.

Military Surgeon, Washington, D. C.

85: 277-364 (Oct.) 1939

Unification of Medical and Dental Education in Basic Sciences. L. C. Fairbank.—p. 277.
Role of Aviation Medicine in Development of Aviation (International Review). A. D. Tuttle and H. G. Armstrong.—p. 295.
Medical Aspects of England's Preparation for Air Attack. D. G. Friend. —p. 301.
Magnesium Trisilicate: Insoluble Antacid and Absorbent Agent for Treatment of Gastrointestinal Disorders in Soldiers and Others. R. C. Page and E. G. Thomas.—p. 307.
Designing and Casting Partial Dentures. T. P. Bull.—p. 315.
Summary of Relation to Aviation of Loss of Intermaxillary Distance. R. A. Lowry.—p. 323.
Management of Acute Abdominal Emergencies. J. M. Waugh.—p. 329.

New England Journal of Medicine, Boston

221: 515-548 (Oct. 5) 1939

Social and Economic Situation of Medical Profession in Sweden. J. Waldenström, Uppsala, Sweden.—p. 515.
Pigment Excretion in Pellagra. A. P. Meiklejohn and R. Kark, Boston. —p. 519.
Allergic Reaction to Insulin: Report of Case. H. Ulrich, S. B. Hooker and H. H. Smith, Boston.—p. 522.
Diagnosis of Various Arthritides. W. Bauer, Boston.—p. 524.

221: 549-592 (Oct. 12) 1939

The United States Marine Hospital, Port of Boston: Massachusetts' Oldest Hospital. J. W. Trask, Chelsea, Mass.—p. 549.
Treatment of Leukoplakia Buccalis and Related Lesions with Estrogenic Hormone. I. T. Nathanson and D. B. Weisberger, Boston.—p. 556.
Reciprocal Pharmacologic Effects of Amphetamine (Benzedrine) Sulfate and Barbiturates. A. Myerson, Boston.—p. 561.
Ventricular Fibrillation as Mechanism of Sudden Death in Patients with Coronary Occlusion. H. Miller, Boston.—p. 564.
Chemotherapy and Serotherapy of Pneumonia. F. T. Lord, Boston.—p. 570.

New York State Journal of Medicine, New York

39: 1899-2004 (Oct. 15) 1939

Study of Stillbirth and Neonatal Death Problem: Based on Analysis of All of Rochester's Cases in 1936. H. C. Soule, Rochester.—p. 1905.
Clinical Experience with Sulfapyridine in Treatment of Lobar Pneumonia. A. Levitt, D. S. Levy and S. J. Jaskiewicz, Buffalo.—p. 1916.
Physiologic Observations Following Induced Convulsions. L. L. Orenstein, New York.—p. 1921.
Diagnosis and Treatment of Diabetes: Use of Protamine Zinc Insulin. F. N. Allan, Boston.—p. 1924.
Induced Pneumothorax and Phrenic Nerve Interruption. B. S. Harwood, Saranac Lake.—p. 1929.
Fatal Prodromal Measles. S. L. Homrighouse and Thistle M. McKee, Amsterdam.—p. 1934.
Prevalence of Coronary Artery Occlusion. A. M. Master, H. L. Jaffe and S. Dack, New York.—p. 1937.
Mild Depressions Cared for by the Family Doctor. Elizabeth I. Adamson, Toledo, Ohio.—p. 1941.
Acute Cerebral Emergencies. O. C. Perkins, Brooklyn.—p. 1949.
Deformities of Ear and Nose Treated by Plastic Surgery. G. H. Cox, New York.—p. 1956.
Experiences with Vaginal Hysterectomy by Clamp Method. M. G. Potter, Buffalo.—p. 1962.
Weil's Disease: Compensable Infection in New York State. E. Farrell, Brooklyn.—p. 1969.
Syphilis of Nervous System. R. B. McGraw, New York.—p. 1973.
Mixed Tumors of Soft Palate. H. Liggett, New York.—p. 1976.

Northwest Medicine, Seattle

38: 363-408 (Oct.) 1939

Pelvic Endometriosis. G. H. Gardner, Chicago.—p. 367.
Shock Therapies in Psychoses. C. W. Mack and B. O. Burch, Livermore, Calif.—p. 370.
*Modified Convulsive Therapy for Involutional Depressive Psychoses. A. W. Hackfield, Seattle, and C. Halvorsen, Steilacoom, Wash.—p. 373.
Types of Deafness. H. C. Ballenger, Chicago.—p. 375.
Acute Traumatic Diaphragmatic Hernia. R. Falk and R. S. Smith, Boise, Idaho.—p. 378.
*Treatment of Botulism: Special Reference to Specific Antitoxin and Respirator from Survey of Sixteen Cases. W. E. Watson, Seattle. —p. 382.
Thymic Asthma. W. M. Whitehead, Juneau, Alaska.—p. 387.
Improved Radiographic Technic for Visualizing Odontoid Process. R. Anderson and E. Burgess, Seattle.—p. 388.
Diagnosis of Syphilis in Neonatal Period. M. L. Bridgeman, Portland, Ore.—p. 389.
Effect of Bile Salts on Bile Acidity. D. Metheny, Seattle.—p. 390.
Motor Disturbances of Gastrointestinal Tract. C. E. Hagyard, Seattle.—p. 391.

Modified Convulsive Therapy for Psychoses.—Hackfield and Halvorsen outline a modified form of convulsive therapy (massive dose plus postconvulsive sedation) adapted to the involutional depressive psychoses. The treatment was necessitated by the high incidence of this psychosis in the upper age brackets and as a means of preventing thoracic vertebral fractures and other complications. The modification was used in thirty-six cases. No preliminary preparation of the patient is necessary, and treatment may be given even after the patient has eaten. It promotes a gain in weight, and its relaxing effect facilitates sleep. Restraints are contraindicated, if the patient is placed on his back with the head flat on the bed and a pillow under the midthoracic region, the upper extremities in adduction, flexion and internal rotation and the lower extremities in full extension and adduction. The recommended dose of from 3 to 5 cc. of metrazol is inadequate. In the modified technic for patients with pronounced depressive-stuporous states the initial dose is 7 or 8 cc.; for those with marked apprehensive-agitated features from 10 to 12 cc. is used. With this dosage the subconvulsive reaction is eliminated; when it is encountered, a second administration with an increase of 2 cc. above the initial dose produces a satisfactory convulsion. Immediately after the convulsion 3 or 4 grains (0.2 or 0.26 Gm.) of sodium amytal intravenously or a hypodermic of one-fourth grain (0.016 Gm.) of morphine eliminates postconvulsive anxiety, uncontrolled thrashing during the postconvulsive stupor, nausea, headache and muscle spasm and effects complete amnesia for the treatment. The patient awakens from this sedation in from one-half to two hours, and he is given a hot bath and an alcohol rub. Throughout the treatment psychotherapy is utilized with appropriate emphasis on any apprehensive features regarding the treatment. The number of convulsions (induced every other day) necessary to initiate a remission varies with the psychopathologic features predominating. Patients in a pronounced depressive-stuporous state may respond with a remission after two or three convulsions, whereas those with hypochondriac symptoms predominantly of the anxiety type with delusional elements require on an average of from ten to twelve treatments. The delusional, depressive and hypochondriac features resolve, but psychotherapy

is required for the anxiety-compulsive elements that remain. If in this type of patient the remission is not satisfactory, a rest of a week followed by another course proves more satisfactory than a prolonged series of continued convulsions. A remission was induced in each of twenty-four private patients, but relapses occurred in two cases, in one of which the condition was successfully controlled by further treatment. Of the twelve state hospital patients nine showed remissions, one of whom relapsed, and three showed improvement.

Treatment of Botulism.—From his experience in treating sixteen cases of botulism, with a mortality of 30.25 per cent, Watson feels that botulinus antitoxin is imperative, regardless of the duration of the symptoms or the time elapsed from the ingestion of the toxigenic food, and furthermore that large initial intravenous doses of antitoxin diluted in dextrose-saline solution with epinephrine added should be followed by repeated intramuscular injections. The total quantity of antitoxin should depend on the severity of the intoxication and the apparent clinical response to treatment. The author believes that purified type-specific antitoxin would be preferable to the unpurified mixed antitoxin that he has used. Uncontrollable reactions and serum sickness were not encountered in the sixteen cases. In seven of the patients there developed respiratory paresis, requiring use of the respirator. One of these patients refused to be placed in the respirator and died, four who were in the respirator for varying periods died, and two completely recovered. The impression is that early arrangements should be made for respirators and that the apparatus should be brought to the patient, as his already weakened condition is aggravated by transportation. It appears to the author that the case mortality in botulism should be reduced from its former standard of from 60 to 70 per cent to a level of 30 per cent or less by the early administration of antitoxin and artificial respiration. These patients should be observed closely for clinical evidence of progress of the disease, and severe toxicity manifested by dysarthria, dysphagia, dyspnea, cyanosis, atelectasis or persistent vomiting should be considered a grave prognostic sign.

Ohio State Medical Journal, Columbus

35: 1033-1152 (Oct.) 1939

Treatment of Nephritis. H. O. Mosenthal, New York.—p. 1049.
Diagnosis of Acute Surgical Abdomen in Children. A. W. Carley, Dayton.—p. 1056.
Regional Ileitis. J. W. Holloway, Cleveland.—p. 1059.
Treatment of Gas Gangrene. E. P. McNamee, Cleveland, and C. R. Lukenski, New York.—p. 1062.
Functional Sterility in Women. B. B. Rubenstein, Cleveland.—p. 1066.
Tumor Clinic of Cincinnati General Hospital: Record of Its First Decade. W. M. Millar and Minnie Landen, Cincinnati.—p. 1609.
Diagnosis, Prognosis and Treatment of Hodgkin's Disease. C. S. Higley and H. Hauser, Cleveland.—p. 1075.
Midline Cerebellar Tumors. H. E. LeFever, Columbus.—p. 1080.
Muscle Balance in Routine Refractions. F. B. Fralick, Ann Arbor, Mich.—p. 1083.
Psychosomatic Considerations in "Essential" Hypertension. D. M. Palmer, Columbus.—p. 1087.
Role of Cardiac Output in Congestive Heart Failure. J. McGuire, Cincinnati.—p. 1092.

Pennsylvania Medical Journal, Harrisburg

43: 1-112 (Oct.) 1939. Partial Index

Workmen's Compensation and Occupational Disease Laws in the Commonwealth of Pennsylvania. M. Behrend, Philadelphia.—p. 18.
Abdominal Pain on Locomotion in Rheumatic Disease: Its Significance in the Past Medical History. V. A. Digilio and J. A. Pescatore, Philadelphia.—p. 33.
Aplastic Anemias: Causes, Types and Treatment. J. A. Kolmer, Philadelphia.—p. 36.
*Prevention of Shoulder Dislocations During Convulsive Therapy in Schizophrenia. A. M. Rechtman and N. W. Winkelman, Philadelphia. —p. 39.
Maternal Mortality in a Small General Hospital: Study of the Fifteen Year Period, 1923-1938. F. J. Pearson, Bethlehem.—p. 41.
Some Remarks in Judgment of Blood Bank System for Transfusion. H. Fox, Philadelphia.—p. 49.
Federal Participation in Medical Care: A Suggested Plan. F. A. Riemann, Parkesburg.—p. 52.
Chronic Osteomyelitis Symptomatically Relieved by Intravenous Injections of Hydrochloric Acid. G. S. Backenstoe, Emmaus.—p. 56.
*Propadrine Hydrochloride in Treatment of Allergic Manifestations. J. A. Murphy, Philadelphia.—p. 65.
Treatment of Parkinsonian Syndrome. F. M. Forster, Boston.—p. 67.

Prevention of Shoulder Dislocations During Convulsive Therapy.—Rechtman and Winkelman devised a support for preventing dislocations of the shoulder in schizophrenic patients during convulsive attacks induced by metrazol. The support prevents abduction of the shoulder joint during the initial phase of the convulsive attack when the arms are forcibly and violently abducted. With the use of their belt support they have had no further shoulder dislocations. The support consists of a pelvic band not unlike a polo belt. A pair of wrist cuffs are fastened through loops to the lower strap on the pelvic band. A pair of forearm cuffs are fastened through loops to the canvas belt so as to allow sufficient room for making the injection into the vein at the elbow. The pelvic belt is attached firmly, but not tightly, to the patient before the injection is given. The wrist and forearm cuffs are closed with the arm into which the injection will be made held in supination.

Propadrine for Allergic Manifestations.—Murphy used propadrine (phenyl-propanol-amino-hydrochloride), one of many synthetic compounds offered as a bronchodilator and local vasoconstrictor, in the treatment of approximately 200 patients with bronchial and nasal allergies. Dose for dose the clinical relief closely paralleled that of ephedrine, with untoward side effects definitely less although not entirely absent. The tremor, tachycardia, insomnia, occasional nausea, retention of urine in the elderly man and sense of muscular weakness so frequently observed with the use of ephedrine, necessitating combining it with a sedative, were not evident when propadrine was used. The three-eighths grain (0.024 Gm.) recommended by the distributors of the drug was less satisfactory as a starting dose than three-fourths grain (0.05 Gm.), except in children. Propadrine has not been found efficacious in the severer episodes of asthma and hay fever, but under these conditions, as with ephedrine, it was more apt to aid hay fever than asthma.

Physiological Reviews, Baltimore

19: 439-578 (Oct.) 1939

Effect of Toxemia on Metabolism. E. Holmes, Cambridge, Mass.—p. 439.
Present Status of Barbiturate Problem. A. L. Tatum, Madison, Wis. —p. 472.
Muscle Hemoglobin. G. A. Millikan, Cambridge, England.—p. 503.
Architecture of Viruses. W. M. Stanley, Princeton, N. J.—p. 524.
Fat Transport in Animal Body. W. R. Bloor, Rochester, N. Y.—p. 557.

Public Health Reports, Washington, D. C.

54: 1807-1846 (Oct. 6) 1939

Stabilized Method of Forecasting Population. B. D. Karpinos.—p. 1807.
Studies of a Filter-Passing Infectious Agent Isolated from Ticks: V. Further Attempts to Cultivate in Cell Free Mediums: Suggested Classification. H. R. Cox.—p. 1822.
Influence of Transplanted Normal Tissue on Breast Cancer Ratios in Mice. J. J. Bittner.—p. 1827.

54: 1847-1876 (Oct. 13) 1939

Cultivation of Phase I Haemophilus Pertussis in Semi-Synthetic Liquid Medium. J. W. Hornibrook.—p. 1847.
Development and Genetic Characteristics of Adenomatous Stomach Lesion in Strain I Mice. H. B. Andervont.—p. 1851.
Effects of Extracts of Human Urine on Tumors in Mice. F. C. Turner. —p. 1855.

Review of Gastroenterology, New York

6: 366-453 (Sept.-Oct.) 1939

Some Differential Diagnostic Problems in Borderlands of Gastro-Enterology and Cardiology. J. S. Rodman and W. G. Leaman Jr., Philadelphia.—p. 366.
Perforated Carcinoma of Stomach Complicated by Streptococcus Sepsis: Case. F. W. Bancroft and H. N. Vermilye, New York.—p. 382.
Value of Stirling Test in Diagnosis of Peptic Ulcers. M. Einhorn, New York.—p. 386.
*Treatment of Duodenal Ulcer with Histaminase: Preliminary Report. J. R. Nakada, St. Louis.—p. 389.
Causes of Poor Results in Operative Treatment for Duodenal Ulcer. H. R. Owen, Philadelphia.—p. 394.
Anemias versus Gastrointestinal Disease. S. A. Loewenberg, Philadelphia.—p. 402.
Surgical Management of Acute Intestinal Obstruction. L. F. Knoepp, Beaumont, Texas, and J. R. Phillips, Houston, Texas.—p. 411.
Intestinal Distention. J. Fine and A. Starr, Boston.—p. 419.
Chronic Ulcerative Colitis Complicated by Carcinoma. M. J. Matzner and G. Schaefer, Brooklyn.—p. 422.
Gastrointestinal Symptoms in Sodium Chloride Privation. B. Jablons, New York.—p. 427.
Conservatism in Surgery of Pancreas. G. W. Papen, Boston.—p. 432.
Red Blood Cells in Obstructive Jaundice. E. Foldes, New York.—p. 438.
*Prognostic Value of Cholesterol Partition Study. D. A. Meiselas, Brooklyn.—p. 441.

Treatment of Duodenal Ulcer with Histaminase.—Nakada treated seven patients who had duodenal ulcer with histamine hydrochloride detoxifying substance or histaminase. The subjective symptoms (pain, nausea, belching and nervousness) were promptly relieved in all the patients. Temporary recurrences of symptoms were due to intercurrent infections in two patients

and to faulty cooperation in two others. However, each improved again on recovery from the intercurrent infection or on resumption of cooperation. Histaminase promises to be of considerable value in the treatment of duodenal ulcer, provided future studies give like results. The method of procedure was to keep the patient on a diet free of condiments, alcohol, fatty or fried foods, dressings, thickened gravies, pastries and excessively sweet foods. Coffee was allowed once a day. Nicotine was reduced as much as possible. One ampule of histaminase (containing 1 detoxicating unit of histamine hydrochloride) was given intramuscularly three times a week and one tablet (containing 5 units) was prescribed three times a day one hour before meals. The patients were usually given one or the other first for a week or two. An additional tablet was taken if the patient awoke at night. The rapidity with which the dosage can be reduced and finally eliminated depends on the progress of the patient. After treatment is discontinued, the patient should be examined clinically and roentgenologically about every six months until all objective evidence has disappeared.

Cholesterol Curve in Liver and Gallbladder Diseases.—Meiselas emphasizes the diagnostic and prognostic value of the cholesterol ester curve in cases of jaundice in determining the severity and likelihood of recovery in liver and gallbladder disease. He does not wish to imply that other laboratory tests of hepatic function should be dispensed with but claims that the cholesterol test should be used as an adjunct to them.

South Carolina Medical Assn. Journal, Greenville

35: 243-268 (Oct.) 1939

Nonspecific Treatment of Ozena. G. R. Laub, Columbia.—p. 243.
Some Considerations of Wound Healing. W. H. Simmons Jr., Charleston.—p. 248.
Diverticula of Small Intestines. A. E. Baker, Charleston.—p. 250.

Southern Medical Journal, Birmingham, Ala.

32: 983-1076 (Oct.) 1939. Partial Index

Force Fluids: Evaluation of and Indications for Fluids in Disease. V. E. Simpson, Louisville, Ky.—p. 983.
Widespread Misuse of Endocrine Products in Treatment of Gynecologic Symptoms. G. Penick, Oklahoma City.—p. 994.
Treatment of Infant Vulvovaginitis with Estrogenic Hormone. J. C. Weed and C. G. Collins, New Orleans.—p. 1000.
*Use of Testosterone Propionate in Impotence: Clinical Studies with Male Sex Hormones: III. T. A. C. Rennie, S. A. Vest Jr. and J. E. Howard, Baltimore.—p. 1004.
Treatment of Cancer of Larynx with Comparison of Results Obtained by Surgery and Radiation Therapy. M. F. Arbuckle, St. Louis.—p. 1008.
Hypertensive Factor in Wilms' Tumor. W. E. Daniel, Charlotte, N. C.—p. 1014.
Wilms' Tumors: Embryonal Adenosarcomas of Kidney. L. W. Long, Jackson, Miss.—p. 1016.
Method of Application of Skeletal Traction for Treatment of Contracture of Knee. D. H. O'Donoghue, Oklahoma City.—p. 1023.
Mucoid Carcinoma of Breast. C. E. Gillespie and H. C. Schmeisser, Memphis, Tenn.—p. 1029.
Recent Psychologic Approaches to Patients with Alcohol Problems. R. V. Seliger, Baltimore.—p. 1049.
Protamine Zinc Insulin: Some Reasons for Occasional Dissatisfaction with Its Use. B. F. Keltz, Oklahoma City.—p. 1058.
Pathologic Nasal Conditions Affecting Clinical Allergy. J. S. Agar and A. Cazort, Little Rock, Ark.—p. 1063.

Testosterone Propionate and Impotence.—None of eight patients with psychic impotence that Rennie and his co-workers treated with injections of testosterone propionate reported improvement. No change in symptoms was observed in a male homosexual patient similarly treated. If the factor of suggestion is ruled out it seems unlikely to the authors, in spite of other reports, that in states of psychic impotence specific testis hormones in doses adequate for excellent responses in hypogonad patients offer any therapeutic help.

Wisconsin Medical Journal, Madison

38: 841-932 (Oct.) 1939

The Challenge to Medicine. R. G. Arveson, Frederic.—p. 857.
Indigenous Malaria. L. M. Morse, Neillsville.—p. 864.
Ear Injuries. W. E. Grove, Milwaukee.—p. 869.
Simplified Infant Feeding Formula: Report of Use of Irradiated Evaporated Milk and Water in 2,004 Cases. H. O. McMahon, Milwaukee.—p. 874.
Regional Enteritis: Relation of Its Onset, Clinical Course and Pathologic Manifestations to Its Cause. J. A. Bargen, Rochester, Minn.—p. 877.
Transposition of Viscera with Asymptomatic, Arrested Cardiac Development: Case Report. R. E. Garrison, Wisconsin Rapids.—p. 882.
Vaginal and Perineal Trauma. J. W. McGill, Superior.—p. 884.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Annals of Rheumatic Diseases, London

1: 249-366 (Oct.) 1939

Treatment of Rheumatic Diseases in the United States and the Continent of Europe. W. S. Tegner.—p. 249.
Gout an Unsolved Problem. J. B. Burt and R. G. Gordon.—p. 304.
*Effect of Chrysotherapy on Sedimentation Rate in Rheumatoid Arthritis. W. Goldie.—p. 319.
Erythrocyte Sedimentation Test: Wide-Bore Tube Method Using Oxalated Blood and Permitting Correction of Result to Standard Red Cell Volume. D. H. Collins, H. J. Gibson, J. Race and H. B. Salt.—p. 333.
Index of Sedimentation Rate on a Mathematical Basis. L. J. Cuthill.—p. 359

Effect of Gold Therapy on Sedimentation Rate in Arthritis.—Goldie discusses the effect of gold salt therapy on the blood sedimentation rate in 400 cases of rheumatoid arthritis. The patients have been under observation for from six months to four years. The blood sedimentation rate has been determined before and at the end of each course of treatment. On humanitarian grounds a control series has been observed. Gold treatment produced a marked fall in the blood sedimentation rate, and the higher the initial figure the greater the fall. While the initial figure is valueless from a prognostic point of view, the change in the blood sedimentation rate is of definite value. The greater the fall and the lower the final figure, the better, on an average, was the clinical result. The mean fall in the rate was entirely determined by the fall taking place at the end of the first course of treatment. Reduction of dosage should take place after the first course. The blood sedimentation rate was of little value in anticipating either relapse or severe toxic reactions. The most severe upsets occurred in the presence of a normal rate. The utility of the test is thus considerably lessened from a practical point of view.

Archives of Disease in Childhood, London

14: 181-278 (Sept.) 1939

Osseous Dystrophy Following Icterus Gravis Neonatorum: Generalized Osteitis Fibrosa with Areas of Pigmentation of Skin and Precocious Puberty in the Female. Frances Braid.—p. 181.
Epiphysial Necrosis in Pituitary Gigantism. E. Traub.—p. 203.
Dysostosis Multiplex: Pfaundler-Hurler Syndrome: Report of Two Cases. D. Engel.—p. 217.
Monocytic Leukemia in Childhood. D. Court and D. G. F. Edward.—p. 231.
Vitamin A Requirements of Infants: Health of Infants Fed on Roller-Process Dried Milk, With and Without a Supplement of Vitamin A. Helen M. M. Mackay.—p. 245.
Review of Twenty Years of Breast Feeding in Liverpool. Margaret Robinson.—p. 259.
Inguinal Hernia in Female Twins, with Special Reference to Identification of Monozygotism. C. E. Kellett.—p. 265.
*Renal Lesions in Children with Erythema Nodosum. A. Wallgren.—p. 271.

Renal Lesions in Erythema Nodosum.—Wallgren encountered three children with erythema nodosum in whom acute hemorrhagic nephritis appeared simultaneously with the cutaneous eruption. All three children were tuberculin sensitive, and it is thought that the tuberculous infection directly or indirectly played a part in the occurrence of the erythema nodosum. In one of the cases pronounced primary pulmonary tuberculosis was present at the same time. Assuming that subclinical renal changes in erythema nodosum might be much more common than can be gathered from the limited number of clinically obvious cases, the author examined by the Addis method the urine of eighty-eight children with erythema nodosum. A pathologic erythrocyturia was demonstrable in about every third or fourth child. After the disappearance of the erythema and the accompanying fever the urine became normal again. The renal lesions occurred in children who did not display the least evidence of a complicating throat infection and just as often in those with negative as in those with positive tuberculin reactions. Therefore there is no reason for assuming either that a tuberculous or that a streptococcic infection is a requisite condition for the occurrence of pathologic erythrocyturia. Tests showed that in children with erythema nodosum there is often capillary fragility during the erythema nodosum fever. This capillary fragility occurred with about the same frequency in children with pathologic erythrocyturia as in those in whom this sign was not present. Capillary fragility is thought to be due to a toxic

action on the vascular endothelium. The renal lesions are probably to be regarded as an expression of the same remote toxic or allergic action of the infectious agent as that which produced the eruption of erythema nodosum and the capillary fragility of the skin.

British Journal of Dermatology and Syphilis, London

51: 405-450 (Oct.) 1939

Growth of Epithelium in Tegumentary Tissues. H. Leslie-Roberts.—p. 405.
Keratoderma Blennorrhagicum; Review of Condition, Its Clinical Features and Its Treatment, with Report of Three Cases and New Method of Treating Skin Lesions. N. S. Taylor.—p. 418.
Pathogenesis of Keratosis Blennorrhagica. E. Epstein.—p. 428.

British Medical Journal, London

2: 713-752 (Oct. 7) 1939

Intracranial Causes of Headache. H. Cohen.—p. 713.
Headache as Early Symptom of Nervous and Mental Disorder. D. Curran.—p. 717.
*Results with Epanutin in Mental Hospital Patients. Susannah Davidson and J. D. Sutherland.—p. 720.
Treatment of Irreducible Intussusception Due to Meckel's Diverticulum. R. Stuppel.—p. 722.
*Diagnosis and Treatment of Infantile Mastoiditis. P. W. Leathart.—p. 723.

Diphenyl Hydantoinate for Mental Disorders.—Davidson and Sutherland have recently use sodium diphenyl hydantoinate (epanutin) in the treatment of twelve epileptic patients with mental symptoms. The drug was administered by gradual replacement of the drug already in use. Most of the patients were more than 40 years of age and had a long history of hospitalization and correspondingly long treatment with drugs. They were almost all admitted for psychotic behavior as well as fits. The most prominent result of the treatment was the appearance of toxic effects; in eight of the twelve patients they occurred within a few weeks. The toxic effects included headache, giddiness, nausea, loss of appetite and ataxia. Rashes developed in three patients. These effects have already been referred to in connection with this preparation, but their frequent and early appearance obviously restrict the use of the drug, for though some are possibly not serious in themselves they antagonized these patients. The three youngest patients showed no toxic effects. Only one patient showed mental improvement, but this lasted for only a few weeks, after which he lapsed into the former state. This patient also showed a temporary improvement on a change from soluble phenobarbital to methyl-ethyl-phenobarbital or vice versa. The effect of the change to sodium diphenyl hydantoinate was rather more marked. His relapse followed the recurrence of fits. It would appear that in his case, as in some of the others, this drug makes a useful addition to those on which patients can be maintained for a few weeks. The absence of sedative effect proved an undesirable feature with several patients, as it released the excessive irritability and, in some cases, impulsive behavior which was relieved by other drugs. Sodium diphenyl hydantoinate had little effect on the character and number of fits in most cases. However, there was a balance in favor of this drug. The authors' experience suggests that the drug is of use for the younger and better preserved patients, but owing to its toxic effects it is advisable not to use it for more than a few weeks at a time.

Infantile Mastoiditis.—In 146 recent consecutive necropsies Leathart found that mastoiditis undiagnosed in life had been present on one or both sides in twenty-nine cases. The frequency with which mastoiditis complicates other diseases has not been sufficiently realized. The eustachian tube is more horizontal in children than in adults, and normally it opens with each act of deglutition. Because of this horizontal position any material in the postnasal space finds its way through the eustachian tube into the tympanum and then to the mastoid antrum more easily than in adults, especially if the child is lying on his back while feeding. This anatomic difference shows how easily infected mucus can enter the tympanum from the postnasal space in air-borne diseases and how vomited material may do so in food-borne diseases. As a rule there is no discharge from the ear, and swelling behind it is never present at a stage when treatment is imperative. Moreover, often the child is too young to complain. Nevertheless mastoiditis can be recognized in children at an early stage by the presence of local physical signs other than those usually associated with mastoiditis. If a child suffering from an air-borne or food-borne infection or a wasted bottle-fed infant does not improve, mastoiditis is likely to be the cause and should always be suspected. The child with an increase in temperature, crying out as if in pain, putting his hand to his head, pulling at his ear or rolling his head on his pillow should suggest mastoiditis. There is one physical sign which is constant. It consists in the presence of a palpable gland or glands in the posterior triangle of the neck behind the sternomastoid muscle. They are small at first but increase in size with the chronicity of the mastoid infection. Other conditions produce enlargement of these glands, but mastoiditis in its catarrhal or purulent stage is by far the most common. An immediate operation is not necessary in every case, for in some instances mastoiditis in its early stage subsides spontaneously. Immediate operation is necessary only for a child whose general condition is not improving and who is losing weight and becoming dehydrated. Children suffering from air-borne infection, diarrhea and vomiting or wasted bottle-fed infants should never be fed while lying down, nor should they be allowed to lie on their backs for any length of time. Frequent turning of these infants has led to a definite decrease in the frequency of mastoiditis as a complication in these diseases and has proved a potent factor in promoting spontaneous recovery in infants as yet not ill enough to require operation. Mastoidectomy will save the lives of about 70 per cent of the children in whom mastoiditis is complicating an air-borne or food-borne infection.

Journal of Laryngology and Otology, London

54: 531-610 (Sept.) 1939

Effects of Airplane Noise on Auditory Acuity of Aviators. E. D. D. Dickson, A. W. G. Ewing and T. S. Littler.—p. 531.
Symptoms, Signs and Treatment of Nasal Sinusitis in Children. S. E. Birdsall.—p. 549.

Lancet, London

2: 773-816 (Oct. 7) 1939

Primary Histologic Lesion of Regional Ileitis. G. Hadfield.—p. 773.
Sulfapyridine in Treatment of Pneumococcus (Type II) Pneumonia. T. Anderson, E. D. Cooper, J. G. Cairns and D. R. Brown.—p. 776.
Pneumonia Treated with Sulfapyridine: Review of 342 Cases. O. Rönche and F. Vogt.—p. 778.
*Defective Hearing and Nutrition in Children. Phyllis M. Tookey Kerridge, Gwendoline Briggs, D. P. Choyce and Janet Hill.—p. 781.
Hernia Through Foramen of Winslow. M. Silverstone.—p. 786.

Defective Hearing and Nutrition in Children.—Kerridge and her associates tested the hearing acuity of sample groups of children in Great Britain who lived under different social conditions. In one series the children were chosen from good environments in private schools, day schools and boarding schools; in another series they were in public elementary schools or in ecclesiastical orphanages. The latter were chosen because they represented institutions which were hard pressed for funds. The children were between 7 and 14. They were tested with a gramophone audiometer. Every child was given a second chance of doing the test before being classed as a failure. Children who failed the second time were tested individually, and in most cases a teacher's report on their mental capabilities was obtained. A medical history was obtained whenever possible. The ears were examined with an auriscope to detect wax; but, since time did not permit of retesting after removing the wax, some of the failures attributed to wax in the ears may have been partly due to middle ear disease. Finally the child was tested with a pure tone audiometer by air and bone conduction for hearing acuity over the auditory spectrum. In this way the amount and the location of the defect to the middle or inner ear could be determined. The authors report their observations on about 1,000 children with good social conditions and on about 6,000 children with poor social conditions. It was impossible to test all the children in both summer and winter. The authors found that housing was of no significance, since even the children in the poor groups were well housed (orphanages). The two series of children did, however, differ greatly in the food they obtained. Middle-ear disease is about four times as common, on the average, under poor social conditions as it is under good social conditions; in the poorest places, whether urban or institutional, it may be nearly ten times as common as in a good environment, nearly a quarter of the child population being affected. Climate, housing and the mixing of children seem to have little effect on the incidence of the disease. The children with the highest incidence of defec-

tive hearing had diets deficient in many factors, but an increase in the food taken by two groups of these children for a year did not reduce the incidence of defective hearing. The figures here given show that probably the most important work on the prevention of deafness will be done by those who are striving to improve the social conditions and, in particular, the nutrition.

Medical Journal of Australia, Sydney

2: 421-456 (Sept. 16) 1939

Diencephalon: Structural, Functional and Clinical Considerations. A. A. Abbie.—p. 421.
Use of Cardiazol in Psychiatry. B. Barry.—p. 430.
Mental Diseases in Relation to General Practice. J. K. Adey.—p. 438.

2: 457-490 (Sept. 23) 1939

Heart Sounds. E. Murphy.—p. 457.
Some Observations on Pelvicephalometry in Late Pregnancy. D. G. Maitland.—p. 465.
Some Statistical Facts Concerning Whooping Cough in New South Wales. E. S. A. Meyers.—p. 468.

Japanese Journal of Experimental Medicine, Tokyo

17: 333-374 (Aug.) 1939

*Virus of Venereal Lymphogranuloma Obtained by Tissue Culture: Culture on Various Mouse Organs and Virulence Tests in Mice. K. Manabe.—p. 333.
*Id.: Development in Cells and Morphology of Virus. K. Manabe.—p. 355.
Studies on Elementary Body of Polyhedral Disease of Silkworm. T. Taniguchi, M. Asano, M. Hosokawa and K. Ishikawa.—p. 363.
Large Scale Cultivation in Vitro of Vaccinia Virus by Aeration of Medium. H. Yaoi and S. Arakawa.—p. 369.

Virus of Venereal Lymphogranuloma.—According to Manabe the so-called Miyagawa bodies after many investigations were identified as the virus of venereal lymphogranuloma. All other investigators who studied these bodies were able to identify them only after staining, but Manabe has been able to observe them also in the fresh living state. He presents two reports, the first dealing with the culture of the virus on various mouse organs and with tests on the virulence and the second dealing with the development of the virus in the cell and with its morphology. He used a modified cover glass method. The plasma was obtained from guinea pigs; the organ extract was prepared from brain, spleen and testes of adult mice, and the organs used for the virus culture were obtained from mice fetuses or from newborn mice. The virus strains to be examined were from the glands of patients whose disorder had been definitely identified as venereal lymphogranuloma. These strains are inoculated into mice. The diseased mouse brain is removed and immediately emulsified with Tyrode's solution (stock emulsion). Several pieces of organs are dipped into this stock emulsion and then are cultured (virus-tissue culture). Regarding his technic of culture, the author says that plasma and organ extract are mixed on the cover glass; the infected pieces of organ tissue are placed in this, and after organ extract is dropped on the tissues the preparation is sealed with paraffin and placed in the incubator at 37 C. Pieces of organs which are dipped for thirty minutes into an emulsion of healthy mouse brains serve as controls. Since it is not sufficient to identify the virus in the tissue culture, animal tests were made to determine the virulence. The studies revealed that the virus of venereal lymphogranuloma can be cultured in various organs from mouse fetuses or newborn mice. The virus develops with equal advantage in epithelial cells and in fibroblasts. Usually a vacuole is formed, which is filled with virus bodies. These bodies increase for four or five days, and then they decrease with the degeneration of the culture tissue. Their virulence increases as their numbers increase and decreases as the culture tissue degenerates. In his second report the author demonstrates that by means of dark field and oil immersion devices it is possible to observe the living virus and its morphologic development in the cell. Comparing stained specimens with living specimens, in which the virus bodies show motility, one can see that the virus of venereal lymphogranuloma develops and gradually increases in the living cell. Finally it breaks through the cell and repeats this process of development in another living cell. The individual virus bodies are readily differentiable. Occasionally two go together in the manner of diplococci, and again several are grouped together. Like Miyagawa and others, Manabe was able to observe differences in the size of the virus bodies.

Presse Médicale, Paris

47: 1381-1396 (Oct. 4) 1934

War Wound Excisions. G. Roux.—p. 1381.
Army Typhus and Its Prevention. P.-F. Armand-Delille.—p. 1383.
*Investigations of Adrenal Insufficiency: Effect of Diet, Vitamins and Certain Other Factors on Survival of Adrenalectomized Rats. W. Weslaw and A. Wroblewski.—p. 1384.

Adrenal Insufficiency in Rats.—Weslaw and Wroblewski report the results of dietetic, vitamin and chemical experiments made on 172 white rats on which adrenalectomy had been performed. Male and female rats weighing from 100 to 330 Gm. were used. Recovery after the operation was rapid and left no lesions. The basic diet consisted of equal parts of cheese and barley and of milk. Brewers' yeast and cod liver oil were administered in specified quantities twice a week and occasionally carrots. The experiments were made in twelve series. The control group of forty rats, representing the entire range of the weight scale, was given the basic diet and showed a mortality of 95 per cent from three to twelve days after operation. Since the investigations were undertaken in part to verify the results of tests made by others with regard to survival medication in renal insufficiency, the negative and positive results of their own tests are carefully presented. No satisfactory results were obtained from the use of lactoflavin-5'-phosphoric acid on eighteen rats or on five other rats in which vitamin C was superadded. Cystine and glutathione employed on ten rats and sodium chloride as well as sodium chloride with sodium bicarbonate employed on other groups were equally unable to prevent loss of weight and vitality and death. Positive results were obtained on seven female rats to whose basic diet rye bread was added immediately after the surgical operation; furthermore, in an experiment with five male rats the basic diet was replaced by wheat bread, vitamin C and cod liver oil. The most remarkable results, according to the authors, were achieved with a regimen consisting of fresh wheat bread, thinly greased with lard, and cheese (Tilsitt). Repeated experiments showed that the loss of weight and the signs of renal insufficiency evolving from the basic diet were invariably and immediately arrested by the addition of wheat bread, lard and cheese and invariably reappeared when this addition was withdrawn. It insured survival for more than 100 days. Sodium chloride added to the milk was of no avail in the absence of the triple combination of wheat bread, lard and cheese, nor was potassium chloride in conjunction with wheat bread, lard and cheese. On the contrary, gain of weight was at once stimulated by the omission of sodium chloride. In another group the mere addition of the cheese, without bread, invariably induced vital restoration and caused the symptoms of adrenal insufficiency to disappear. The authors point out that though rye and wheat bread prolonged the life of the adrenalectomized rats from thirty to forty days, respectively, if given at once after the operation, the former in conjunction with the basic diet, the latter without, these regimens could not prevent death. They also assert that cheese by itself gave practically the same results as the rye bread-lard-cheese combination and may be the enigmatic energizing agent.

Schweizerische medizinische Wochenschrift, Basel

69: 869-888 (Sept. 30) 1939. Partial Index

Experiences with Protamine Zinc Insulin in Young Diabetic Patients. W. Trachsler.—p. 869.
*Significance of Vitamin C in Treatment of Addison's Disease. J. Pojer.—p. 872.
Gas Gangrene After Medicamentous Injections: Deceptive Bactericidal Power of Alcohol. R. Regamey.—p. 874.
Alimentary Hygiene: Investigations on Alimentary Deficiencies Among Children of Lausanne. F. M. Messerli.—p. 876.

Vitamin C in Addison's Disease.—Pojer discusses the relationship between vitamin C and the hormone of the adrenal cortex and also the disturbances in the mineral metabolism during Addison's disease. Assuming a synergism of the cortical hormone and of vitamin C in the human organism and an impairment of this synergism in patients with Addison's disease, the author carefully observed the course of two cases of Addison's disease in which he administered large doses of vitamin C. He was induced to try this vitamin C therapy by a report of Laederich and his associates, who found vitamin C highly effective in a case of Addison's disease which had failed to respond to endocrine therapy and to the administration of sodium chloride. The two cases of Addison's disease in which

Pojer tried vitamin C therapy concerned a man aged 26 and a girl aged 14. In both cases it was possible to detect a vitamin C deficit in the urine. However, after four days of treatment with vitamin C the urinary deficit had disappeared. Patients were given daily twenty tablets (each containing 0.05 Gm.) of a vitamin C preparation; that is, the daily dose was 1 Gm. This medication caused changes in the mineral metabolism, as was indicated by the potassium, sodium and chlorine ions. For a time previous to the onset of the vitamin C therapy the patients had been given 15 Gm. of sodium chloride daily. In both patients the potassium content was increased, the sodium content was reduced, but the chloride content was normal. As a result of the vitamin C therapy, the general condition improved and the cutaneous pigmentation was reduced. In the patient who had been given daily 4 cc. of adrenal cortex extract by intravenous injection, the adynamia was reduced. The author concludes that the great improvement in the patients and the reduction in the pigmentation justify the use of vitamin C in Addison's disease.

Atti d. Soc. Ital. Ostetricia e Ginecologia, Rome

35: 333-444 (July-Aug.) 1939. Partial Index

*Testosterone Propionate in Treatment of Acute Puerperal Mastitis. F. Guercio.—p. 353.
Quinine-Calcium Treatment in Inertia of Uterus with Early Rupture of Membranes. P. Cattaneo.—p. 415.

Testosterone Propionate in Puerperal Mastitis.—Guercio employed testosterone propionate in four cases of acute puerperal mastitis and in one case of chronic mastitis with postoperative lacteal fistula. The patients with acute mastitis stopped lactation as soon as the breast became painful, red and tumefacted. Although the condition was acute in all cases, none of the patients had an abscess when the treatment began. In the only case in the group in which the condition was observed from its onset, a daily dose of 0.01 Gm. of testosterone propionate was administered. The condition rapidly progressed to abscess formation, which was successfully treated by incision and drainage. Three patients were seen within one week from the beginning of the condition. They received a daily dose of from 0.05 to 0.07 Gm. of the substance, up to a total dose of 0.25 Gm. (in four days) or else 0.3 Gm. (in one week). In all cases pain, inflammation and tension of the breast were immediately relieved. In two cases the engorgement rapidly disappeared with consequent disappearance of fever and of the local infiltration. The improvement was moderate in one case of this group, in which mastitis was of the interstitial type. The condition evoluted to abscess formation, which was successfully treated by incision and drainage. The patient who was suffering from chronic mastitis and lacteal fistula had a daily dose of 0.05 Gm. of testosterone propionate for four days. The secretion rapidly diminished. The fistula healed in about ten days. In all cases reported lactation could not be resumed. According to the author the treatment gives satisfactory results if it is given early in the development of acute mastitis and with high doses (from 0.05 to 0.07 Gm. a day up to a total dose of 0.25 Gm. in four days or 0.3 Gm. in one week). Duration of the treatment depends on its effects, as shown by the favorable evolution of the condition. However, because of the fact that high doses inhibit milk secretion, the author advises further work on the subject in order to find the proper dosage by which mastitis can be controlled without causing this inhibition.

Ginecologia, Turin

5: 521-586 (Sept.) 1939. Partial Index

*Surgical Treatment of Stubborn Neuralgia of Bladder. E. Crispolti.—p. 521.
Microscopic Changes of Islands of Langerhans in Some Experimental Conditions (Administration of Dextrose and Insulin). T. Meneghini.—p. 539.

Stubborn Neuralgia of Bladder.—Continuous and persistent pain is the predominant symptom of vesical neuralgia, Crispolti says. It is associated with tenesmus and moderate dysuria. The urine is clear. The symptoms are not related to menstruation. They simulate those of appendicitis, acute abdominal conditions and diseases of the kidney or of the gallbladder. There is no anatomic lesion in or around the urinary tract which can be considered responsible for the condition, which is due to neuritis of the pelvico-abdominal sympathetic plexus. The author points out the utility of Cotte's operation, as modified by Pieri, in the treatment of the condition. The modified operation consists in removing the upper hypogastric plexus and making an exeresis of the lateral sympathetic chains of the first sacral segment. The author reports satisfactory results from the modified operation in two cases. The condition dated back several years in each case. The patients were in a general nervous state. They had had various operations because of erroneous diagnoses (appendectomy and nephropexy). Removal of the upper hypogastric plexus and exeresis of the lateral sympathetic chains of the first sacral segment were followed in both cases by immediate and complete disappearance of pain and of all symptoms, control of the dysfunction of the bladder and disappearance of the nervous condition. The satisfactory results have lasted in the two cases up to the present (almost one year after the operation).

Giornale Medico dell'Alto Adige, Bolzano

11: 309-363 (June) 1939. Partial Index

Change of Blood in Fractures. G. di Castro.—p. 309.
*Pulmonary Tuberculosis and Menstrual Disorders in Puberal Girls. I. Pedrini.—p. 332.

Menstrual Disorders in Pulmonary Tuberculosis.—Pedrini discusses the frequency and clinical significance of menstrual disorders in puberal girls suffering from pulmonary tuberculosis. He observed sixty puberal patients. In a group of fifty-five patients who were suffering from the disease in evolution, forty-four patients complained of menstrual disorders. Amenorrhea existed in thirty-two. The author found that amenorrhea takes place coincidentally with either the development or the aggravation of pulmonary tuberculosis. He believes that its presence is of value first for the diagnosis of pulmonary tuberculosis (when such a diagnosis has not previously been made) and second for ascertaining the evolution of the disease (after a diagnosis has been made). Amenorrhea in pulmonary tuberculosis is secondary to the condition of the lung. It is not related to local conditions of the internal genitalia, which are normal, and it is the manifestation of an organic reaction of defense. Moreover, any treatment which is directed to induce the return of menstruation in the course of the disease is unjustified, erroneous and harmful.

Omnia Medica, Pisa

17: 145-339 (March-June) 1939. Partial Index

Primary Chronic Polyarthritis: Etiopathogenesis. A. Robecchi.—p. 145.
*Transient Fever of the Newborn. A. Taddei.—p. 223.

Transient Fever of the Newborn.—Taddei noted the behavior of the rectal temperature during the first week of life of 152 infants of both sexes born in the Clinica Ostetrica e Ginecologica of Pisa. The infants were placed in three different groups, being allowed to nurse fifteen or forty-eight hours after birth and fasting or twenty-four hours after birth but fed during the day with a total quantity of 80 cc. of a 4 per cent solution of dextrose administered in small portions. The temperature was taken every three hours, day and night. The author found that the rectal temperature of the infant is different from that of the mother (and also of a twin in case there is one). Three hours after birth it diminishes, but in the course of the first day of life it rises again. Noticeable changes occur as a rule by the third day and disappear by the seventh or eighth day of life. The changes may be of any of the following types: (1) transient fever, (2) moderate fever and (3) hypothermia. The alterations of temperature in newly born infants are not associated with the interval between birth and nursing, fasting, the administration of dextrose solution, the more or less intense turgor of the mother's breast, the appearance of fever with milk secretion or of nonpuerperal fever in the first week of puerperium. The results of observations do not support certain etiologic theories of transient fever, especially those which show dehydration of the infant or the passage of toxic substances from the mother to the infant through the milk as causal factors. According to the author there is a physiologic congenital lability of the system of regulation of the body temperature in infants. Changes of the body temperature occur when the lability is associated either with

stimulation of the cerebral thermoregulating centers by disintegrated proteins which are absorbed by the infant's body (the so-called tumor from birth) or with a disequilibrium of hormones from structures which take part in the regulation of body temperature, such as the thyroids, the adrenals and the hypophysis.

Klinische Wochenschrift, Berlin

18: 1109-1140 (Aug. 19) 1939. Partial Index

Nicotinic Amino Acids and Cozymase in Blood. H. von Euler and F. Schlenk.—p. 1109.
Blood Structure and Coagulation. C. Wolpers and H. Ruska.—p. 1111.
Nicotinic Amino Acid Therapy in Lupus Erythematosus. W. W. Kühnau.—p. 1117.
*Vitamin C Blood Level in Relation to Metabolism in Fever. F. X. Hausberger and N. Neuenschwander-Lemmer.—p. 1119.
Limits of Diaphragmatic Movements. A. J. Anthony and M. Broglie.—p. 1126.

Vitamin C Loss in Fever.—Hausberger and Neuenschwander-Lemmer record their clinical observations of the behavior of vitamin C in the blood plasma of febrile patients (pneumonia, sepsis, pyelitis), an outgrowth of research studies on the connection between vitamin C and the redox potentiality of the blood and organs in animals and in both healthy and febrile persons. They describe the method employed to determine the vitamin C content and the results of preliminary tests on normal controls. They found that intravenous injections of 10 mg. per kilogram of body weight of ascorbic acid measured at regular intervals were succeeded by a steady diminution of vitamin C in the blood, irrespective of whether the original vitamin C level was high or low. Five minutes after injection, on the average, only 5.4 mg. per hundred cubic centimeters was detected in the blood and after twenty-four hours only 0.48 mg. This diminution may be due to the action of the kidneys (after a lapse of two and one-half hours, 324 mg. of injected ascorbic acid was found in the urine out of 700 mg. administered, the blood level reaching a low value of 1.33 mg. per hundred cubic centimeters), or to the oxidation of the acid or to the rapid absorption by the tissues (the presence of ascorbic acid was observed electrometrically in the nonvascular epidermis two minutes after injection). The analysis of similar doses administered to febrile persons indicated a vitamin C loss in the blood level 24 per cent below that of healthy persons, a 4.1 mg. per hundred cubic centimeter loss on the average. After two and one-half hours the vitamin C blood level was often similar to that preceding injection. The confirmatory evidence of the urine showed that whereas healthy persons excreted as much as 50 per cent within the first hour, febrile patients voided only 15 per cent (78 to 100 mg. out of 600 to 650 mg. injected). The authors attribute this loss of vitamin C to its rapid disintegration in the blood or to tissular absorption. An accelerated vitamin C decomposition in the blood of febrile persons is attested by the fact that while ascorbic acid administered to healthy persons undergoes oxidation slowly, a larger proportion of the amount administered to febrile persons disappears within the same time limits. The same vitamin C impairment was observed by the authors in two cases of artificial fever and one of degeneration of the cardiac muscle. On the other hand, febrile persons subjected for a longer time to vitamin C dosage before the blood level test was made reacted to the test in the same way as healthy persons. The authors are in accord with the view that infectious diseases continuing for some time involve a heightened vitamin C loss and, in consequence, necessitate a heightened vitamin C regimen.

Medizinische Welt, Berlin

13: 1183-1216 (Aug. 26) 1939. Partial Index

Adnexitis and Appendicitis. G. Hasselhorst.—p. 1183.
Problem of Endometriosis. H. Petri.—p. 1185.
*Modern Prophylaxis of Measles. H. Grod.—p. 1192.
Roentgenologic Studies in Gastro-Enterostomy Without Simultaneous Subtotal Resection of Stomach. F. Kern and H. E. Büttner.—p. 1194.
Acceleration of Erythrocyte Sedimentation Speed in Aged and in General Arteriosclerosis. O. Schreurer and H. O. Hagenmeyer.—p. 1195.
Early Treatment of Mastitis. A. Poerschke.—p. 1197.

Prophylaxis of Measles.—Grod first reviews experiences with convalescent serum and with serum from adults and then discusses the use of a mixed serum obtained from retroplacental blood. He employed the latter serum in the course of an epidemic of measles. It was administered to 170 children in doses of from 15 to 20 cc. In the majority of children the serum was injected on the fourth or fifth day of incubation; that is, at the time when the exanthem appeared. To eight children it was given earlier and to three not until the sixth day of incubation. After excluding the cases in which exposure to measles was not absolutely certain and also those which had not been observed for a sufficient length of time, there remained forty-four cases which were suitable for the evaluation of the efficacy of the serum made from retroplacental blood. In 47.7 per cent of these cases complete protection could be obtained, in 36.3 per cent the severity of the disease was noticeably weakened and in 16 per cent it was not influenced. The author points out that these figures correspond to those obtained with serum from adults. The serum from retroplacental blood was well tolerated by the children. Placental extract, when given under the same conditions and in identical doses, was found to have the same therapeutic effect but was not so well tolerated as the serum from retroplacental blood.

Monatsschrift für Kinderheilkunde, Berlin

79: 147-306 (Aug. 14) 1939. Partial Index

Gastrointestinal Ulcer During Childhood. E. Wegener.—p. 147.
Contribution to Problem of Tolerance for Morphine in Nurslings. U. Grüninger, I. Graby and A. C. Ohling.—p. 169.
Pathogenesis of Acetone Vomiting. W. Goeters.—p. 176.
Complete Closure of Abdominal Aorta by Thrombosis During Childhood. W. Becker and H. Girgensohn.—p. 180.
Aspects of Lupus Pernio. H. Kohl.—p. 191.
Value of Ide's Chromatic Reaction in Diagnosis of Congenital Syphilis. G. Ernandez and D. Jonas.—p. 196.
Electrocardiographic Reactions in Pylorospasm. E. Limper.—p. 202.
*Evaluation and Treatment of Incontinentia Alvi During Childhood. H. Oegg.—p. 230.

Incontinence of Feces in Children.—Oegg gives detailed clinical histories of three children with incontinentia alvi. The first patient was a boy of almost 9 years and the two others were boys of about 6 years. The author is convinced that functional nervous factors on a psychogenic basis played an important part in the development of the incontinentia alvi, as all of these children lived in an environment that was unfavorable for their psychic as well as physical welfare. After thorough evacuation of the bowel, psychotherapy together with dietetic measures produced cure within a comparatively short time in all three cases. X-ray examination following a barium sulfate enema revealed in all changes in the large intestine. Dilatation was noticeable not only in the region of the ampulla and of the sigma but also in the colon. X-ray examinations of the hand were made for two of the children, and in both of these the bones showed pathologic changes. The diet had been unsuitable in all three of the children. The author assumes that the unsuitable diet produced intestinal changes, which played a part in the pathogenesis of the incontinentia alvi. This assumption becomes even more probable when it is considered that the bones likewise exhibit changes indicative of former malnutrition. The author thinks that the changes in the colon are probably the result of changes in the tonus and motility of the colonic musculature, which in turn are caused by disturbances in the sympathetic nervous system. Although hereditary and mental factors may be the basis, the author is convinced that unsuitable nutrition is the factor that leads to the manifestation of the incontinence of feces.

Röntgenpraxis, Leipzig

11: 461-532 (Aug.) 1939. Partial Index

*Spondylitis Infectiosa and Its Differentiation from Osteomyelitis, Tuberculosis of Spinal Column and Degenerative Diseases of Intervertebral Disks. H. Bade.—p. 461.
Differential Diagnosis of Juxta-Articular Bone Foci. T. Börsch.—p. 475.
Differential Diagnosis of Benign and Malignant Gastric Tumors. W. Dieker and E. Fahrner.—p. 486.
Rare Form of Diaphragmatic Hernias (Parasternal Hernia). Erika Ellinger.—p. 490.
Spontaneous Gastroduodenal Fistula. F. Eggs.—p. 502.
Calculary Occlusion of Choledochus After Operation on Gallbladder. K. H. Volbeding.—p. 505.
Looser's Zones of Transformation in Femur. H. Schmitt.—p. 509.

Differential Diagnosis of Spondylitis Infectiosa.—Bade shows that spondylitis infectiosa occurs after many different infectious diseases such as scarlet fever, measles, smallpox, influenza, malaria and typhus, after infections with pneumococci, staphylococci and streptococci, and after brucellosis. He reports

ten cases of spondylitis infectiosa. He regards as characteristic a narrowing of the involved intervertebral disk. This narrowing generally does not involve the entire intervertebral disk but frequently only a sector or a half. The adjoining portions of the diseased vertebrae show small irregularities and defects and a more dense structure. In the reported cases the fine osseous foci developed as a rule only after the narrowing of the intervertebral disk. Especially typical for infectious spondylitis is the rapid appearance of reactive proliferations of bone which develop into marginal pads and bridging bands. The differentiation of spondylitis infectiosa from osteomyelitis of the spinal column is easy in the severe acute cases, which often terminate in death before the changes become roentgenologically demonstrable. Subacute and chronic cases of osteomyelitis with sclerosis of the involved vertebra are differentiable from spondylitis infectiosa by roentgenoscopy, as are also those cases in which the roentgenogram discloses areas of fused bone tissue. However, there are chronic cases of osteomyelitis in which the roentgenogram discloses the same narrowing of the intravertebral cleft and the small defects on the terminal plates of the vertebrae as is the case in spondylitis infectiosa and thus a differentiation merely on the basis of the roentgenogram is impossible. The differentiation from tuberculosis of the vertebral column is usually readily accomplished merely on the basis of the x-ray examination. But in the cases in which the roentgenogram is not sufficient for this purpose, the clinical aspects and especially the course will permit a diagnostic decision. In difficult cases, specimens of pus should be inoculated into guinea pigs. It should be remembered that even in spondylitis infectiosa gravitation abscesses may develop, although they are less frequent than in tuberculosis and osteomyelitis of the vertebral column. Another disorder that must be considered in the differential diagnosis is osteochondrosis of the intervertebral disks. This degenerative disease also causes narrowing of the intervertebral disks and sclerosis of the adjacent portions of the bodies of the vertebrae, that is, a picture develops which greatly resembles the terminal stages of spondylitis infectiosa. However, in osteochondrosis the narrowing is uniform throughout the intervertebral disk, defects of the terminal plates are absent and loosening of the structure of the intervertebral disk may cause dislocation of adjoining vertebral bodies.

V 113
1939

Zeitschrift für Immunitätsforschung, Jena

90: 193-360 (Aug. 31) 1939. Partial Index

*New Investigations on Immunity in Venereal Lymphogranuloma: Existence of a Special Reactivity Characteristic for Each Group of Receptive Tissues, Determining Evolution of Infection. J. Caminopetros.—p. 217.
Influence of p-Aminobenzenesulfamide and of Similar Compounds on Anthrax. G. Ivánovics.—p. 252.
Experiences with Protective Inoculation in Combat of Diphtheria in Beograd. S. Ramsin.—p. 255.
Experiences with Colloidal Gold Test According to Borowskaja. H. Schubert.—p. 267.
Practical Significance of Serologic Examination, Especially of Complement Fixation Reaction, for Diagnosis of Weil's Disease. W. Gaehtgens.—p. 287.

Immunity in Venereal Lymphogranuloma.—Caminopetros tested several series of patients who had adenitis or rectitis by the injection of antigen or of virus into the glandular tissue and into the rectal mucosa or the perianal vegetations. These tests were always complemented by the inoculation of virus and by the search for virus-neutralizing substances in the serum of the patients. Further he investigated whether the specific antigen injected into the vein or under the skin of new subjects, several times a week and for a long period, would provoke the appearance of virus-neutralizing substances in the blood or cutaneous allergy and whether by this procedure the organism could be protected against experimental infection. At the same time he investigated, on the one hand, the preventive action of the serum of convalescents against experimental infection of rabbits and, on the other hand, the curative action of such a serum in cases of rectitis or adenitis. On the basis of his observations, the author concludes that in venereal lymphogranuloma each receptive tissue possesses a reactivity to the infection which is peculiar to it and which determines the characteristics and the evolution of the infection: cure of adenitis in from six to eight months, extremely long persistence of rectitis, and rarity of lesions in the female genitalia in spite of the long persistence of the virus. The general immunity conferred on the organism by adenitis as well as by rectitis has no influence whatever on the local infection. This immunity, which is manifested by the cutaneous allergic reaction and the refractory state of other receptive tissues (groups of glands) distant from the focus of infection, must be attributed to the direct action on these tissues of the virus circulating in the blood at the onset of the infection. On the other hand, the injection of antigen (several times each week over a long period) can produce neither the appearance of a general refractory state nor cutaneous allergic reaction and cannot protect the organism against experimental infection. In the search for virus-neutralizing substances in the blood, it was found that the threshold was extremely low in rectitis as well as in old cases of adenitis even after inoculation of virus or of antigen. The serofloccultation is not as clearly positive as during the period of inguinal infection. Furthermore, the serum of patients in whom the disorder has existed for a long time has no prophylactic action against experimental infection in rabbits. Such serum seems to have no influence on the evolution of adenitis or rectitis. On the other hand, the injection of antigen into the diseased tissues of adenitis or rectitis exerts a noticeable curative action and can be used in their treatment.

Khirurgiya, Moscow

1-160 (No. 6) 1939. Partial Index

Healing of Wounds and Nourishment. A. Z. Kordoba.—p. 3.
Nitrous Oxide in Surgery. M. I. Sakharov.—p. 16.
New Gas Anesthetic—Cyclopropane. P. M. Starkov.—p. 26.
*Complications of Spinal Anesthesia. M. A. Egorova.—p. 37.
Experimental Data on Pathogenesis of Shock. N. I. Bobrik.—p. 46.
*Blood Transfusion in Extensive Burns. V. I. Struchkov.—p. 53.

Complications of Spinal Anesthesia.—Egorova reports 128 cases in which operation was performed under spinal anesthesia in the gynecologic and surgical services of the Moscow Clinical Institute. These patients did not present any lesion of the nervous system prior to the operation; 35.7 per cent were free from any complication after the spinal anesthesia, while 64.3 per cent presented a variety of symptoms pointing to the irritation of the meninges. Of these, 10 per cent had a mild transient headache, 13.5 had a headache combined with nausea and vomiting and occasional occipital rigidity and 24.3 per cent had headaches accompanied by a meningeal symptom complex. Syncope took place in 2.4 per cent, involvement of cranial nerves in 3.2 per cent, sphincter disturbances in 13.8 per cent, diminution or loss of tendon reflexes in 15.6 per cent, paresis of the lower extremities in 4.6 per cent and trophic lesions of the skin in six cases. The duration of the symptoms varied from a few days to several weeks, and in a few cases with involvement of the conus caudae from several months to years. The author concludes that the clinical reaction of the human organism to the introduction of anesthetizing substances into the subarachnoidal space is of the meningeal type, with occasionally deeper involvement of the brain substance and the roots. These complications were not associated with preexisting nervous lesions. Microscopic studies of a patient dying eighteen hours after gastric resection, from a hemorrhage, revealed the presence of definite leptomeningitis and epiduritis of the spinal cord. The author concludes that spinal anesthesia cannot be regarded as entirely safe and its complications as innocent. The indications and contraindications for its use must therefore be carefully weighed.

Blood Transfusion in Extensive Burns.—Struchkov reports 242 cases of extensive burns treated by the open method. Thirty-seven of the patients presenting shock, grave sepsis or retarded healing were given one or more blood transfusions. The age of the patients varied from 6 months to 63 years. There were nineteen children. The mortality rate in the children's group was 10.5 per cent, whereas among the children treated without blood transfusion it was 19 per cent. Eight patients were given transfusions while in a state of shock. All of these recovered. Of the twenty-four given transfusions during the suppurative septic stage, a striking improvement was noted in twelve, a satisfactory result in eight and no effect in four. In two of the latter conserved blood from nephritic patients was used. Transfusion of fresh citrated blood during the septic

suppurative state had the effect of removing the toxic manifestations. The temperature sharply declined, the appetite improved, and the patients felt stronger and began to gain weight.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

83: 4493-4608 (Sept. 16) 1939

Humeroscapular Periarthritis. H. E. Rookmaker.—p. 4494.
*Hematuria, Renal Colic and Formation of Acetylsulfapyridine Calculus After Treatment with Sulfapyridine. I. Snapper, S. H. Liu and H. L. Chung.—p. 4501.
Treatment of Menopausal Disturbances. M. Scholtens.—p. 4508.
Picrotoxin in Poisoning with Barbituric Acid. R. A. Hoekstra and A. J. B. Poortman.—p. 4513.
Case of Superfetation. D. K. Heeringa.—p. 4515.

Hematuria and Renal Calculi After Sulfapyridine.—Snapper and his associates describe four cases of hematuria after treatment with sulfapyridine. In the first patient, a man aged 35, and in the fourth patient, a child aged 22 months, the hematuria developed without local symptoms. In the second patient, a youth aged 19, the hematuria was accompanied by renal colics, which were apparently caused by dilatation and spasm of the left pelvis and ureter. The probable cause of the hematuria and pain was precipitation of acetylsulfapyridine crystals in the urinary passages, as was confirmed by the postmortem examination in the fatal (third) case. In this case, the treatment with sulfapyridine caused hematuria but no renal colics. The necropsy revealed a small calculus in the renal pelvis. Examination disclosed that the calculus consisted of a compound of sulfapyridine, probably acetylsulfapyridine.

Acta Medica Scandinavica, Stockholm

102: 1-162 (Sept. 23) 1939. Partial Index

*Aspiration Biopsy of Liver, with Remarks on Its Diagnostic Significance. P. Iversen and K. Roholm.—p. 1.
Successful Treatment of Giardiasis in Man with Acranil—a Hydrochloride of a New Acridinic Compound. P. de Muro.—p. 17.
*Influence of Vomiting and Nausea on Renal Function. J. Clausen.—p. 22.
Biliary or Duodenal Reflux in Acute Necrosis of Pancreas. J. Bottin.—p. 31.
Studies on Sulfate Clearance. T. Bjering and E. Ølgaard.—p. 55.
Aspect of Coagulation of Blood: Method of Determination of Coagulation Time. E. Hecht.—p. 79.
Electrocardiogram in Chronic Aneurysm of Heart. O. Nordenfelt.—p. 101.
*Disturbance of Sugar Metabolism After Acute Carbon Monoxide Poisoning. S. Moeschlin.—p. 140.

Aspiration Biopsy of Liver.—Iversen and Roholm developed a method of aspiration biopsy of the liver by which an amount of tissue sufficient for microscopic examination is obtained They use a simple trocar consisting of a cannula 18 cm. long and 2 mm. wide and a pointed stylet. The free edge of the cannula is sharp and notched. By turning the cannula on its axis, while it is pushed into the liver, a cutting effect is obtained. The authors introduce the cannula in the posterior axillary line in the ninth intercostal space, just below the lower arch of the last digitation of the serratus anterior, thus passing through the complementary pleural space and the diaphragm before reaching the liver. Before the aspiration, the skin is painted with iodine and anesthesia is produced with a 2 per cent solution of procaine hydrochloride with epinephrine. The anesthesia is effective within two minutes; this interval is used to teach the patient to hold his breath after deep expiration. After the skin is pierced the trocar is pushed in till its tip meets the upper surface of the diaphragm, which moves in breathing. The trocar is then withdrawn a little so that it is clear of the diaphragm. The patient is told to breathe deeply about four times, stopping with deep expiration and fixation of the chest. The last part of the procedure should be carried out quickly, but it should not be commenced before expiration is completed. The trocar is pushed through the diaphragm and into the liver for about 2 cm. The stylet is withdrawn and a record syringe (10 cc.) is attached to the cannula. A vacuum is produced by pulling the piston as far back as possible; the cannula is forced from 1 to 2 cm. into the liver, while the syringe is rotated at the same time. The cannula is quickly withdrawn, and the operation is complete. The authors resorted to this form of biopsy 160 times. It proved successful in 22.5 per cent of the cases. The method involves little inconvenience for the patient, but the risks involved are still somewhat uncertain. For this reason, the indications for its employment cannot be definitely decided as yet. Tendency to bleeding is a contraindication. The method makes it possible to demonstrate the presence of acute and chronic inflammatory conditions, tumors, degenerative processes, obstruction to the flow of bile and other conditions. The method is helpful not only in the diagnosis but also in the prognosis.

Influence of Vomiting and Nausea on Renal Function.—In the course of tests on the renal function Clausen occasionally noticed an essential shift in the ratio of urea clearance to creatinine clearance in direct connection with nausea and vomiting, and so he decided to investigate this problem. He cites experiments which demonstrate that medicamental or mechanical production of nausea and vomiting gives rise to considerable changes in the function of the kidneys. Nausea and vomiting diminish the renal function, and this decrease does not affect the excretion of all substances equally, urea clearance being lowered relatively more than creatinine clearance. This lowering of the renal function is not dependent on changes in the blood pressure, as no decrease of the blood pressure was found during the periods in which the renal function was lowered. The decrease in the renal function coincides with a pronounced decrease in the diuresis. Although this decrease in diuresis may by itself result in falling clearance values, it will influence the urea clearance and the creatinine clearance in the same manner, so that it cannot be the cause of the observed fall in the urea-creatinine clearance ratio. Nevertheless, the author thinks that the abrupt fall in diuresis contributes in some way to produce this fall in the ratio. He thinks that the decrease in creatinine clearance and urea clearance may be due either to changes in the glomerular filtration (due to local circulatory disturbances) or to changes in the activity of the tubular cells, whereas the shift in the ratio between urea clearance and creatinine clearance can be explained only by an increased reabsorption of urea in the tubules of the kidney. The author concludes that these studies are of practical significance as they indicate that caution is necessary in the evaluation of tests of the renal function if nausea and vomiting appear while the tests are being carried out.

Sugar Metabolism After Carbon Monoxide Poisoning.—The fact that glycosuria is observed after carbon monoxide poisoning induced Moeschlin to examine the sugar content of blood and urine and the diastase content of the urine in all cases of acute carbon monoxide poisoning. In some of these cases he also investigated the sugar content of the cerebrospinal fluid and the course of the blood sugar curve during tolerance tests. He made his investigations in thirty-five cases of acute carbon monoxide poisoning, excluding all cases in which there were no definite signs of intoxication and those in which more than twenty-four hours had elapsed since the intoxication. In 57 per cent of the cases the blood sugar was noticeably increased following the intoxication. The increase in the blood sugar content generally persisted for from twenty-four to forty-eight hours, but in two cases it persisted three days and in one case eight days. The previous existence of a diabetic component was definitely excluded by later tests. There was no parallelism between the severity of the intoxication and the degree of increase in the sugar content of the blood; however, the incidence of hyperglycemia was greater with severe than with mild intoxication. Glycosuria was observed in only 17 per cent of the cases. The sugar content of the cerebrospinal fluid proved noticeably increased in eight of eleven cases. The diastase content of the urine was not increased after carbon monoxide poisoning. The most interesting changes were observed in the blood sugar curves, the majority of which were pathologic. Some had the typical diabetic outline, with steep increase in the blood sugar, absence of a double peak and retarded decrease, whereas others had a steep and high increase with a comparatively rapid decrease. Repeated control tests revealed that the changes decreased rapidly, so that after a few days or a week normal curves were seen. The author was able to corroborate the appearance of leukocytosis following acute carbon monoxide poisoning, and he found that this leukocytosis is more frequent than hyperglycemia. He believes that the disturbances in the sugar regulation are caused by a central impairment, but he is unable to decide whether this impairment is due to the direct toxic action of the carbon monoxide or to hypoxemia.